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INTRODUCTION TO PHYSIOLOGY

TO MY WIFE

INTRODUCTION TO PHYSIOLOGY

BY

W. H. NEWTON
D.Sc., M.D.
Holt Professor of Physiology, The University, Liverpool

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PREFACE

MANY branches of knowledge must be studied before the details of physiology can be fully mastered, and experience shows that this may considerably damp the enterprise of the general reader. The professional student is often no less discouraged. He has undergone the necessary preliminary training, but physiology does not follow logically on the systems of knowledge he has just studied. He tends on the one hand to doubt their usefulness to him and on the other to seek vainly for the central idea of the subject. It may have been rash to try to meet the wishes of the general reader and the difficulties of the professional student in the same book, but the attempt seemed worth making, and I have received every encouragement from the publishers.

The obstacle which all beginners have to overcome is that the idea permeating and cementing the whole of physiological knowledge is the unity of the body. It is impossible to grasp this without a knowledge of the working of its parts, and so a vicious circle exists. The object of this small book is to break the circle by displaying the body working as a whole right from the outset, and placing the first details in perspective against this background. It is hoped that in this way the student will pick up essentially physiological ideas from the beginning and escape the frustration which may accompany the perusal of " preliminary " facts.

No one can know all the facts. The serious student needs to know a great many, but he needs first a conception around which to arrange them. The general reader is only interested in them in so far as they help him to understand what the subject is all about; at all events, that is the first thing he wants to know. I have explained to him in simple language, which I hope will not alienate the serious student, those fundamental scientific ideas which I think he may find difficult. As a compensation for this slur on the extent of his knowledge, I have drawn freely on his intelligence and power of imagination where the body itself is concerned. If he will look at and feel his own body and observe the people around him, and perhaps glance occasionally in the window of a butcher's shop, he will find the little anatomy he needs to know presented more effectively and interestingly than would be possible in pages of print. Those parts of the subject which cannot possibly be understood without specialised knowledge I have simply left out. The book does not pretend to cover the whole of physiology at an elementary level. It is an introduction to the subject, intended to inculcate a " physiological " outlook, and other considerations have been subordinated to this end. In contrast to some topics which are but lightly touched upon, the critical reader will find others which it has been possible to treat in more detail than might have been expected.

I believe that first steps in physiology can be given the life and fascination which are presupposed by the nature of the subject, and that the way to do it is through an approach of this kind. In spite of its imperfections I hope that every medical student will read this book during his first term of physiological study. I hope also that those responsible for teaching physiology to senior forms in schools, to nurses and to students of physiotherapy, will consider carefully the advantages of this way of presenting it. The extent to which they use the book or prescribe it for use is a matter for individual taste, but I trust that the general idea will not fall altogether on stony ground. To my friend the general reader I give no advice, but I shall eagerly observe his response.

I am greatly indebted to my wife, not only for carefully reading the manuscript and proofs, but for much guidance as to the placing of emphasis and the limits of what the reader might be expected to stand. It is a pleasure to acknowledge the help of Mrs. H. W. Hughes in typing the manuscript, and the patience and encouragement of Mr. T. Clare in questions relating to the production of the book.

W. H. NEWTON

1947

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Units of Measurement

1 kilogramme (kgm.) = 1000 grammes (gm.)
1 milligramme (mg.) = 1/1000 gramme
1 microgramme (μg.) = 1/1000 milligramme
1 litre (l.) = 1000 cubic centimetres (cc.)
1 millisecond (msec.) = 1/1000 second (sec.)
1 calorie (cal.) = heat needed to raise 1 gm. water through 1°C.
1 kgm.-calorie = 1 kilocalorie = 1 Calorie = 1000 calories

The energy needed to lift 1 kgm. through 1 metre = 1 kgm.-metre
1 kgm-calorie = 426 kgm.-metres = 3086 foot pounds

Conversion Factors

1 kilogramme = 2.20 pounds
1 litre = 1.76 pints
1 metre = 39.37 inches

To convert °C. into °F., multiply by 9/5 and add 32.
To convert °F. into °C., subtract 32 and multiply by 5/9.

°C.	°F.	°C.	°F.
10	50	35	95
15	59	40	104
20	68	45	113
25	77	50	122
30	86	100	212

CHAPTER I

THE FIRE OF LIFE

THERE is a peat fire in the north of Yorkshire which is said never to have gone out for 100 years. It has probably been visited by thousands who, as they gazed at it, felt a little wonder, a little awe, and some comfort. Why should its glow signify more than that of another fire?

The reason lies in the length of time. "*Never once*," thinks the sightseer, "has that fire been quite extinguished since it was lit more than a century ago," and his mind dwells on the ceaseless tending it has received. How many long-lived fires after 5, 10, 20 or 50 years must have stolen a march on their custodians and quietly expired? He thinks, perhaps, that those who looked after this particular fire must at times have been lucky—have caught it on the point of death. No family could be so infallible as never once to forget it. The fire is the living witness of a remarkable feat; not of a momentary effort, but of a sustained devotion able to uplift even the mind which contemplates it. Yet each spectator is himself a fire, which he expects to burn for at least 70 years, and he has no need to go out of his way to see others. Should he close his eyes for 10 seconds in a busy street, he will bump into several and probably make them burn a little faster in consequence.

The fires of life do, in fact, burn rather slowly. In one day a man consumes the equivalent of only a pound of coal, or three-quarters of a pint of petrol. Imagine a pound of coal lasting for 24 hours and you gain an idea of the slow burning of fuel in the body. Recollect, on the other hand, that an 8 horse-power motor car can travel for 4 miles on three-quarters of a pint of petrol, and you realise what a small amount of fuel can do when some of its energy is diverted to work. A small car of this kind may weigh as much as 10 men, and if three-quarters of a pint of petrol can carry the weight of 10 men 4 miles, it should carry one man about 40 miles.

This is surprisingly like the distance a fit man *can* walk in a day if he really tries, but he cannot burn his fuel so quickly as a car burns petrol, so he takes 16 of the 24 hours instead of 6 minutes. He can speed up his combustion to 10 or more times the usual rate for a short time, say in a sprint, but he cannot keep that up for long. In any consecutive 24 hours he is never likely to burn more than twice his average daily quantity of fuel.

But we are travelling too quickly. The reader is already asking questions. What, exactly, do we mean by " burning "? Can fuel produce both *heat* and *work*? What is the fuel? Why should we burn it faster when we sprint than when we lie down? We have often felt hot, but have attributed this to the weather, the temperature of the room, or to hard work. Even when it has been hard work, we have felt rather that the work was doing something to us than that we were actively consuming part of ourselves. If we are doing so, where does the burning take place? We seem to remain much the same shape and size from one day to another, so that at least our outside must represent the fireplace rather than the fire—but where does the outside stop and the inside begin?

These are some of the questions which physiologists ask and, by experimenting, try to answer. A peculiarity of the body is noticed—for instance, its being warmer than its surroundings—and a series of questions promptly arises. But before we have gone very far in answering them, we find the way blocked by the need to investigate some other feature which was thought to be independent, such as the flow of blood in the blood vessels. In this second investigation, a similar interruption occurs, and so on, *ad infinitum*. If a single question could be answered fully and in absolute detail, we should gain a picture of the working of the whole body. This idealised approach is not consummated in practice, for several reasons. Some investigators notice one thing, some another, some a third, and all ask and simultaneously try to find the answer to their own particular question. It is often found, therefore, that our secondary question has been someone else's primary question, and that the answer is already waiting for us to use. On the other hand, a second or third order question might be impossible to answer because some weapon of research is not yet available. William Harvey proved that the blood passed from the arteries to the veins; but the discovery of the minute channels (capillaries) which connect these vessels, and the vistas of enquiry thereby opened up, were denied to him because he had no microscope able to make the capillaries visible. Only in 1661, four years after he died, were they described by an Italian, Malpighi, who was not born until 1628, the very year in which Harvey had made known his original discovery.

Although the history of scientific discovery is thus apparently haphazard, we have no need to follow its random steps. Much of the pattern of physiology is already displayed. We shall, therefore, take advantage of the store of knowledge which has been accumulated for us, a little here, a little there, and consider our questions as they arise. We shall then have the very best reason for launching ourselves into any topic—namely, that it has become necessary for us to discuss it. Let us return now to the matter of combustion, answering our questions in the most convenient order.

1. What is the fuel? In answer, we are safe in saying that *if combustion is really going on* (a matter we shall discuss in succeeding paragraphs) then the fuel must be the food we eat. No other combustible material goes into us, and we are not steadily losing weight as we should were the actual stuff we are made of being consumed. Many questions about the details of the process remain to be asked and answered, but they would lead to an extensive digression which we must postpone.

2. May we describe food as being " burnt "? Strictly speaking, combustion, which is nearly always rapid oxidation[1], is accompanied by light and heat, but the body does not emit light, neither can any be seen on opening it and looking inside. Heat, on the other hand, is produced. The body is warmer than its environment, and the internal organs are warm to the

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[1] A general term for the combination of substances with oxygen. It may also occur slowly, as in the rusting of iron. Rust is oxidised iron. Carbon dioxide is oxidised carbon. Water is oxidised hydrogen. Carbon and hydrogen are important constituents of food, coal and petrol.

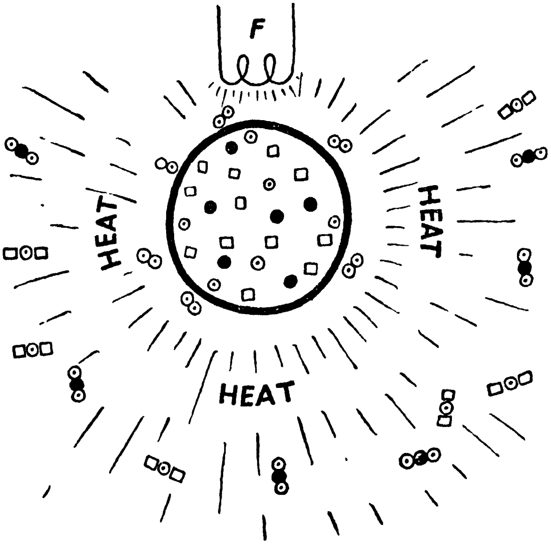

FIG. 1. The combustion of carbohydrate.

●	Carbon atom.
⊙	Oxygen atom.
□	Hydrogen atom.
□⊙□	Molecule of water.
⊙●⊙	Molecule of carbon dioxide.

The atoms inside the black line represent numerically those present in a molecule of grape sugar, but no attempt has been made to arrange them according to the correct structure of the molecule. Just outside the black line are the molecules of oxygen with which the sugar combines on burning. F is the electrically heated filament which is necessary to start the combustion. Once started the action *produces* heat.

touch. Moreover, with one or two exceptions (where the process is incomplete) the final results of the oxidation of food in the body and of its combustion outside are the same. For instance, if butter or cane sugar be ignited by a red-hot electric wire, it burns completely, evolving light and heat, using up oxygen, and turning into carbon dioxide and water vapour (fig. 1). Exactly the same end products are formed in the body, but at a slower rate, and without the emission of light. The utilisation of oxygen, instead of being direct and almost explosively rapid, is retarded, and oxygen is dispensed to the tissues little by little, after having been passed from one molecule to another through the fluids of the body. Instead of going " all at once, and nothing first " like Oliver Wendell Holmes's " one-hoss shay ", the " fuel " smoulders away for a long time. The *total quantity* of heat evolved by a given weight of butter or sugar is the same as if it has been fired by an electric current, but in the body it is consumed so slowly that its temperature never rises above blood heat. With certain reservations in our mind, therefore, we may allow ourselves to speak of food being " burnt " in the body.

3. Thirdly, we have the problem: **Can fuel produce both heat and work?** Petrol ignites so suddenly in the cylinder of a motor car that a large quantity of carbon dioxide and water vapour is produced instantaneously which violently pushes the pistons along. A certain amount of *obvious* heat is produced directly from the explosive burning of the fuel, and a certain amount of work is done by the moving pistons. But the story does not stop there. The pistons rub the sides of the cylinders, and there is friction at the junction of the pistons with the connecting rods, and the connecting rods with the crankshaft; friction in the gears and back axle; and friction between the tyre and the road (fig. 2). As the car moves, it has to push through the molecules of air at the cost of still more friction. In a vehicle going at a constant speed along the level the work of the engine is all devoted to overcoming the frictional resistance of its working parts and of the air. Friction, however, itself produces heat. When half a pint of petrol has taken a vehicle a certain distance, it is found that the total of the

"obvious heat" evolved in the engine, plus all the heat produced secondarily in the frictional parts, is the same as would have been generated if the fuel had simply been burnt in a dish.

A convenient way of thinking of *energy* is as something in

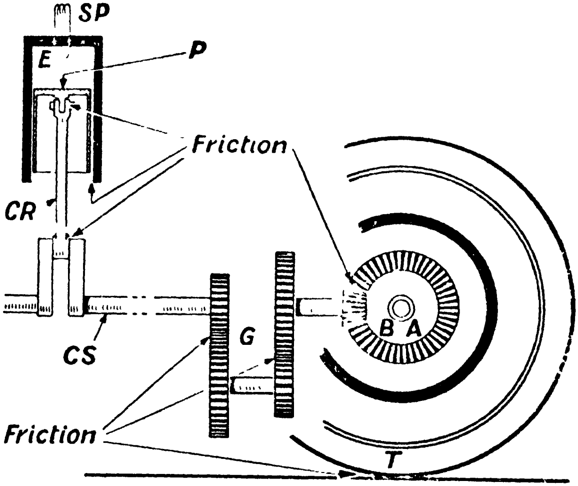

FIG. 2. The utilisation of energy by an automobile.

SP, sparking coil to initiate the explosion E which drives the piston P. CR, connecting rod. CS, crank shaft. G, gears. BA, back axle. T, tyre.

a system enabling it to do useful work but which sooner or later turns into heat. It is customary to say that petrol and coal possess "chemical" energy. When they are oxidised, the energy may all appear quite obviously as heat (as in a fire), or some of it might be capable of doing mechanical work first (as in the petrol engine). Even if it all first appears as heat, it may be possible to trap some of the heat temporarily and make it do work before it is released (as in the steam engine); 25 to 30 per cent of the available energy of fuel can be made to do work in a petrol engine and 20 per cent in the best steam engines. These machines are designed for work, and that proportion of the fuel (the greater part) which provides only heat is wasted. Therefore that engine uses its fuel most efficiently which is capable of diverting the greatest proportion of its total final heat production through a phase of work, and the fraction

$$\frac{\text{heat equivalent of work done}}{\text{total heat production}}$$

is a measure of the *efficiency* of the engine.

This is a simplified presentation of the problem. Sometimes the appearance of the heat equivalent of the work done by an engine is indefinitely delayed. The essence of transport along the ground is the overcoming of friction, and since this gives rise directly to heat, our balance sheet is complete at the end of the journey. Even the energy which goes into " getting the load moving " reappears as heat in the last few yards of the journey, because when the engine is shut off, the momentum initially imparted to the load will now expend itself in overcoming a corresponding amount of friction. In a stationary engine used to lift weights, matters are a little different. If, through the medium of a rope and pulley, an engine lifts a heavy stone to the top of a high building, it will be found that the heat produced in the engine and the pulleys is *less* than would have been evolved by simply burning the quantity of fuel used. If, however, a careless workman pushes the stone off the building and it falls into the street, the heat of its friction through the air plus the friction of its impact with the ground plus the friction of the molecules of air while they are being jostled into sound waves, will be just enough to balance our account. If the stone remains at the top of the building, it is said to have " potential " or stored energy. The original stored (chemical) energy of the petrol has been partly dissipated as " obvious " heat in the engine, and partly diverted through a phase of work, but only part of this work has been used in overcoming friction: the remainder has been put into a deposit account at the top of the building where it may remain for hundreds of years. In stating the efficiency of the engine, the heat which the stone *could* produce by falling is, of course, credited to the engine.

We are now in a position to answer our question about heat and work in the body—in fact the reader has probably already guessed the answer. The fuel burns, and its chemical energy all appears *ultimately* as heat (or as potential energy). When mechanical work is to be done, some of the energy is made first to cause movement. If a man is simply doing "knees full bend" repeatedly, or some other stationary gymnastic exercise, the movement produces friction *in* the body, and the resulting heat goes into the body. So, of course, does the heat which the oxidation of the necessary fuel produces directly—analogous to the "obvious heat" evolved by engines. The final result, therefore, is the same as if the fuel had been burnt in the body without causing movement. But there is an important new point to be considered. *If the man had not performed his exercise, he could not have burnt additional fuel. Muscular activity represents the only voluntary means we have of increasing the rate at which the fire of life burns.* This may be very important in a cold climate.

If the man is pushing a lawn-mower, much of the heat arising secondarily out of the movement appears *outside* the body, from friction of the shoes with the ground and in various parts of the machine, though, as before, there is friction also within the body.

In Chapters XIII and XVI, we shall answer the quantitative questions which naturally follow, i.e., How much fuel. . . . ? How much heat. . . . ? How much work. . . . ? Meanwhile, certain facts have already emerged. At rest, in an equable outside temperature, we keep warm. The fire of life is, therefore, burning steadily, though we are doing no work. Directly we begin to work, the fire burns more rapidly. The energy of the additional fuel we consume cannot by any means all pass into mechanical work before it finally appears as heat. It is like the energy of the petrol of a motor car, or the coal of a locomotive. We may assume that 75 to 80 per cent of it becomes heat inside the body and only 20 to 25 per cent is available for driving the lawn-mower, the friction of whose working parts completes its conversion into heat.

Where does the outside end, and the inside begin?

There is really no answer to this question because all the cells[1] of the body use fuel, including those of the skin. Some cells use fuel faster than others and the outer cells of the skin happen to

[1] Cells are the ultimate microscopic units of which the body is built.

be among those which use it slowly, but so are the cells of bone. The question of inside and outside really does not arise. No part of the body is burning fuel at such a rate that adjacent parts need to be protected. The fact that some parts produce more heat than others is unimportant, since the blood which circulates to every part of the body is very effective in equalising the distribution of temperature. We shall see, however, that the outer layers of the body can cut down their blood supply so considerably that they do make a kind of protective covering which is a bad conductor of heat and helps the underlying parts of the body to conserve heat. In performing this function its temperature is intermediate between that of the surroundings and the temperature of the rest of the body. Only in this sense, and not in the sense in which we first introduced the idea, is there an outside and inside to the body so far as combustion is concerned.

CHAPTER II

THE TEMPERATURE OF THE BODY

Heat in general

AN electric current passing through a wire makes the wire hot. Such a wire is incorporated in an immersion heater, which, when plunged into a vessel of water and turned on, heats the water. The same immersion heater, connected to the same electric supply and turned on for the same length of time must always provide the same amount of heat.

When it is immersed in a jug of water, the heat is transmitted to the water next to it, which expands, i.e. a certain weight of water in this part of the jug now takes up more space—it becomes, therefore, less dense than the surrounding fluid and rises to the surface. Cold water thereupon takes its place, becomes heated and moves on in its turn. All the water in the jug circulates and gradually warms up. This movement is described in detail because we need to refer to the process again—it is *convection*. The water heats the jug by contact (*conduction*), and the jug warms the air by convection, and surrounding objects by radiation. *Radiation* is the direct transfer of heat through space from a warm body to a cooler one and needs the intervention of no material. The sun warms the earth in this way. If the jug is dull black, it will radiate a lot of heat. If it is white or polished copper or silver, it will radiate much less.

Heat is provided by the heater at a greater rate than it is lost by the surface of the jug, so the water becomes hotter and hotter, and finally boils. A pint jug of water may boil in, say, seven minutes, but a two-pint jug will not be boiling after that time *although it has received the same amount of heat.* It is found, however, that the double volume is heated during the same period of exposure through approximately half the number of degrees of temperature. In the trial recorded in fig. 3, in which 1 kgm. and 0.6 kgm. of water were boiled in the same vessel with the same immersion heater, it was found that in 10 minutes the larger volume rose from 15°C. to 59°C., i.e. through 44°C., and the smaller volume in the same time from 15°C. to 87°C., i.e. through 72°C. 0.6 times 72 is 43.2—very close to 44. The reason for the small discrepancy is that no precaution was taken in these experiments against loss of heat, and although heat was *supplied* at the

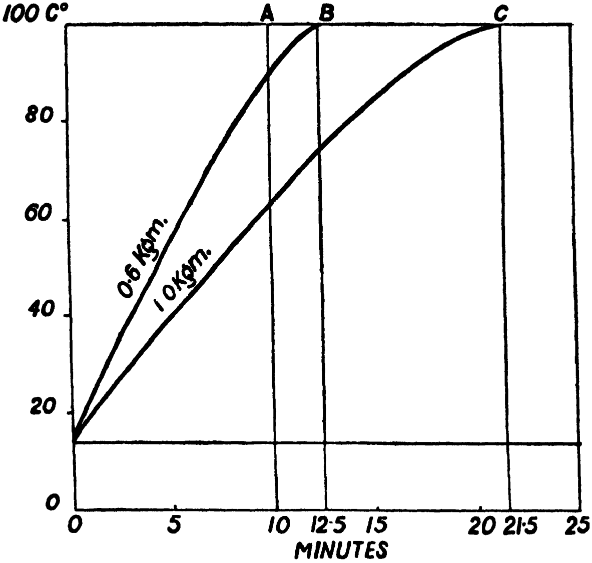

FIG. 3. Graphs showing the rise in temperature (vertical scale) with lapse of time (horizontal scale) of (*a*) 0.6 kgm. of water and (*b*) 1 kgm. of water heated by the same immersion heater in the same vessel.

The vertical line A is to enable the temperatures at the end of ten minutes to be read. B and C show the times at which the respective samples boiled. The horizontal line represents the initial temperature.

same rate by the heater in each case, it was being lost faster by the smaller volume on account of its higher temperature.

If we call the quantity of heat required to raise a kilogram of water (1.76 pint) through 1°C. *one kilogram-calorie* (no heat being lost), we can compare the *amounts* of heat retained by different samples. For instance, a kilogram of water having risen from 15°C. to 59°C. with no precautions against loss must have received 44 kilogram-calories more than it has lost and 0 6 kgm. of water having risen from 15°C. to 87°C. has gained 43.2 kilogram-calories.

If the immersion heater is removed, the jugs of water cool down, at first rapidly, because there is a great difference between their temperatures and that of their surroundings, later more slowly as this difference is diminished. The process of cooling down is, of course, merely the loss of heat by convection and radiation which we have described, and by other methods we have not described.

The principal method we have not yet mentioned is *evaporation.* It is a curious fact that, although 1 kgm.-calorie of heat will raise 1 kgm. of water through 1°C., *540 kgm.-calories are needed to change 1 kgm. of water to its vapour without changing its temperature at all.*[1] Now, unless the atmosphere is quite saturated with moisture, which is very rarely, water vapour is always being removed from any exposed surface of water by the air which, as it were, tries to become saturated. The warmer the air, the more water vapour it can take. Vapour is actually forced into it if the water is heated. Every gramme of water vaporised removes 0.540

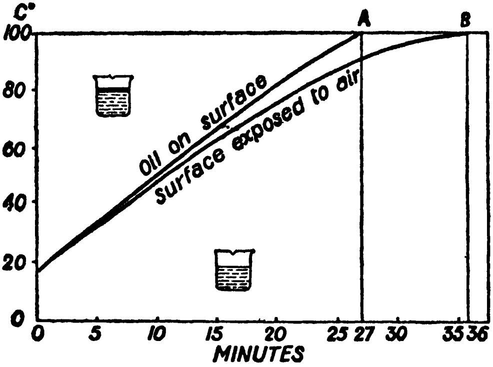

FIG. 4. The rise in temperature (vertical scale) with lapse of time (horizontal scale) of 1 kgm. of water heated with an immersion heater with the surface freely exposed to air (lower curve) and with the surface covered with oil (upper curve).

The vertical lines A and B show the times at which the water boiled in the two experiments.

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[1] Full explanation of this is beyond the scope of this book, but we may assume that the heat is required for conversion into the mechanical energy needed to separate the molecules of water from each other.

kgm.-calories from the rest of the water. One kgm. of water at 100°C. (or 2 kgm. at 58°C.) *could* therefore cool down to 16°C. and lose its whole additional store of 84 kgm.-calories of heat by the evaporation of $\frac{84}{0.540} = 155$ gm. of water.

The reason why freely boiling water cannot be raised above 100°C. by the application of more heat is that the rate of evaporation, which has gradually been increasing, is now able to keep pace with the rate of supply of heat; as much heat is removed during a given time by the transformation of water to vapour as is supplied by the heater.

At lower temperatures, if a jug of water is to be maintained at a constant temperature of, say 58°C., then the heater must supply only that much heat per minute as is being lost per minute by radiation, convection and evaporation.

If a layer of liquid paraffin is poured on the water in the jug it checks evaporation from the surface, and it will be found that such a jug (*a*) heats more quickly, (*b*) cools more slowly and (*c*) can be maintained constant in temperature with a less rapid supply of heat than before (fig. 4).

The heat of the body

Have you ever made a jelly? If so, you will know that the beautifully shaped object presented at the table is nearly all water. It is enabled to stand in virtue of a very small amount of gelatine dissolved in it; it may contain only 5 per cent of solid matter. There is nothing surprising, therefore, in the fact that the body is more than two-thirds water in spite of having a quite firm consistency and a definite shape. The significance of this to us at the moment is that we may assume that it takes *about* the same quantity of heat to raise the temperature of a kgm. of " body " as it does to raise a kgm. of water through 1°C. This is a little complicated by the presence of fat and bone, so that a 70 kgm. man actually needs only 57 kgm.-calories (instead of 70) to raise his temperature by 1°C.

Although the temperature of the body remains fairly constant at about 37°C., that of the surroundings does not, so it is impossible to say that the body is an exact number of degrees warmer than its environment. However, let us assume that it is 21°C. higher—an elevation which is quite usual. It is interesting to compute that a 70 kgm. man, starting at room temperature (supposing this to be possible), would require about 57 × 21 or about 1200 kgm.-calories to raise him to his normal temperature—if he lost no heat in the process. 1200 kgm.-calories represents his store of heat.

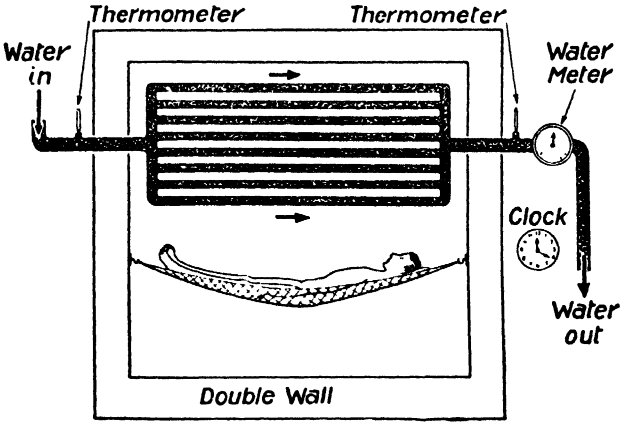

FIG. 5. Apparatus for measuring the heat production of a man over a given period of time. Details of ventilation, etc., are omitted.

A man is continually losing heat to his surroundings, and if he were not warmed all the time by his combustion of food, he would soon cool down to their level. The quantity of heat required per day to maintain the body at an even temperature can be measured. The most straightforward way is to place the subject in a chamber called a *calorimeter* (because it measures calories) whose walls are prevented by electrical devices from transmitting heat inwards or outwards (fig. 5). Now the man inside the calorimeter is losing heat into the chamber, which is cooler than he is. This heat is all absorbed in warming a stream of water which passes through the chamber in pipes. The volume of water flowing through the pipes in a certain time is measured, and its change of temperature is also measured; it is then easy to calculate the number of kgm.-calories it has received. Since it has no other source of heat than the man, and since it is the sole agent for conveying away the heat he has lost, the water gives us the answer to our question. *The man, at rest, loses about 1800 kgm.-calories per day.* As his temperature is still the same as it was when he went in, he must have produced this amount of heat by burning up his food.

If a man's " store " of heat is 1200 kgm.-calories and he loses heat at the rate of 1800 kgm.-calories per day, it looks as though a dead man would reach room temperature (if this were 21° below body temperature) in about 16 hours. In actual fact, he takes longer, because by the time he has lost half his heat he is already cooling much more slowly on account of the lessened difference between his temperature and that of his surroundings. His rate of heat loss becomes less and less as he cools. The living man stays at a constant temperature, and therefore loses heat at a steady rate, provided external conditions do not alter. The two figures showing rate of production and " storage " convey to the reader an idea—as it happens, a false one—of the degree of security or insecurity in which man stands to his environment. His daily income and expenditure (1800 kgm.-calories) appear, at first sight, to be of the same order of magnitude as the capital (1200 kgm.-calories) which he possesses.

When we later consider nutrition in detail, we shall see that man is not so badly off as he seems. A pound of flesh, regarded as modified water, may hold only 2 kgm.-calories of heat, but *if it be burnt like food* to release its " chemical " energy, it may easily provide 3,000 kgm.-calories. This hidden asset can in fact be drawn upon for a long time during starvation, and is the reason why a starving man is by no means a dead man.

Ways and means of adaptation

It is now time we asked how the temperature of the body is kept constant in spite of changing internal and external conditions. The obvious guess is that a man exposed to a lower external temperature consumes more fuel than one exposed to a higher temperature. For an unclothed person below about 28°C. this is true, and the source of heat is muscular activity. We feel much more like walking about and taking exercise when it is cold than when it is hot. Even if we remain still, the muscles[1] tend to become more taut so that the body is tense, and finally they go into the involuntary irregular contractions familiar to us as shivering.

Passing to the higher environmental temperatures we meet an unexpected fact. A naked man, lying motionless, makes just as much heat per hour when the temperature of the room is 34° as when it is 28°. Now if he is consuming the same amount of fuel at these two temperatures, without himself becoming warmer or cooler, it must be because within this range he is able to regulate the speed at which he *loses* heat.

In cold surroundings the layer of skin and fat which invests the body is a somewhat poorer conductor of heat than cork. At an external temperature of 22°C., which is cold to a naked person, the surface of the body is at an average of 30°C. The interior of the body is at 37°C., and this temperature holds good to within about 2 cm. of the surface (fig. 6).

A very different state of affairs exists at an external temperature of 30°C. or so. The blood-vessels of the skin become widely opened, completely neutralising the heat insulating layer of fat, and bringing a rapid flow of blood at 37°C. directly from the interior of the body to just beneath the skin, whose surface, now assuming a higher temperature of about 34°C., is still able to radiate heat to its surroundings (fig. 7).

The skin is not quite " waterproof " and a certain amount of evaporation is always occurring from its surface. This increases as the temperature rises, and, as with the jugs of water, it exerts a certain cooling effect. In the naked man with surroundings above 30°C., the contribution made by evaporation to the losing of heat is enormously increased by the outpouring of sweat upon the skin (fig. 8). This is effected by organs whose special function it is to withdraw water from the blood, and to transfer it to the surface. The blood flowing copiously through the skin is cooled and on its next circuit is

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[1] Muscles are the fleshy covering of the skeleton. They act as the " engines " of the body. They cause movement by changing their shape, i.e., becoming shorter and thicker (see Fig. 39, and pp. 87 and 88).

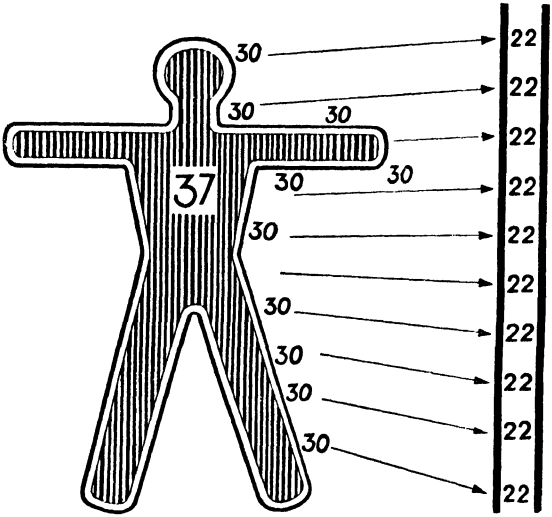

FIG. 6. The maintenance of body temperature in a naked man in cold surroundings.

The body is at 37°C. except for the heat insulating layer which covers it, in which the temperature falls steeply so that the surface is at 30°C. The difference between the surface temperature and the temperature of the surroundings determines the rate at which the body loses heat. The direction of the transfer of heat is shown by arrows.

able to accept more heat from the interior of the body. A diagram of the skin circulation is shown in fig. 9.

We are all familiar with the fact that severe muscular exercise at almost any external temperature causes flushing and sweating. This is because the muscles, in order to do the work required of them, have to produce more heat as a by-product than the body needs to maintain its temperature (see p. 16), and the excess must be got rid of.

To summarise, we now have the following facts about our naked man. The body temperature is maintained at a constant level by a balance between heat production and heat loss. At external temperatures over approximately 28°C. heat production does not fall below a certain minimum rate, but it may rise above this rate when work has to be performed. The temperature of the body in this range of external temperatures is kept down by calling into play certain mechanisms for dissipating unwanted heat, and to these we may add devices under voluntary control, such as the creation of draughts, which assist convection and evaporation. Below about 28°C.

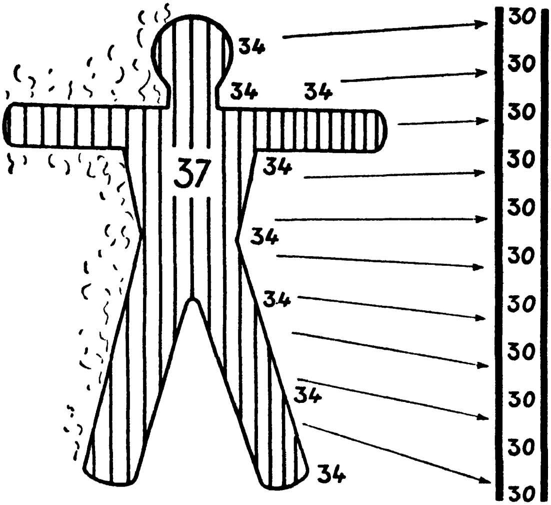

FIG. 7. The maintenance of body temperature in a naked man in warm surroundings.

The diversion of blood to the surface of the body has obliterated the heat insulating layer of Fig. 6, and so raised the temperature of the surface that it is still able to lose heat to the warmer surroundings. The steam rising from the body indicates the participation of evaporation and the lighter shading is intended to suggest the diminution of heat production which may occur as a long term adjustment to a warm climate.

the circulation of blood in the skin is low: the loss of heat can no longer be minimised except by putting on clothes. Initiating muscular contraction and so increasing the production of heat

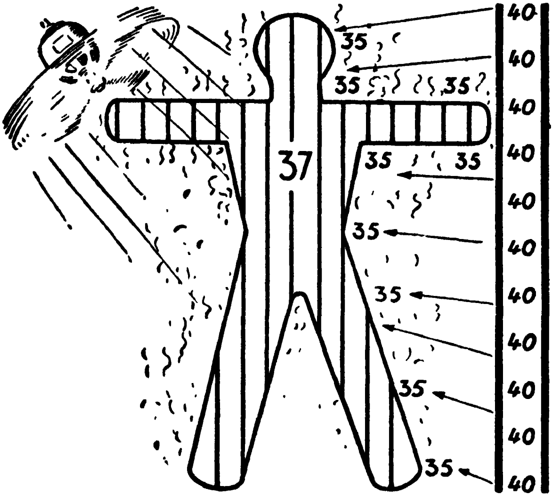

FIG. 8. The maintenance of body temperature in a naked man in hot surroundings.

The difference between the state of affairs represented in this diagram and Fig. 7 is that the surroundings are above body temperature and heat is being transferred from them to the body. Loss of heat is entirely dependent upon sweating, which keeps the surface of the skin below that of the surroundings and of the interior of the body. The object in the corner is an electric fan which moves the air rapidly over the surface of the body, thus preventing it from becoming heavily charged with water vapour which would hinder evaporation.

also allows body temperature to be maintained. We may now add the additional information that unclothed men have succeeded in lying *for a time* quite still and without shivering at temperatures down to 22°C. Between 28° and 22° the transmission of heat by the " outer layer " of the body depends entirely on its physical constitution and not on the rate of blood flow through it, which is already at its lowest. Heat loss, therefore, cannot be further diminished. Since there is no increase in heat production until the subject finally shivers (when it increases considerably), the temperature of the motionless naked subject falls slowly.

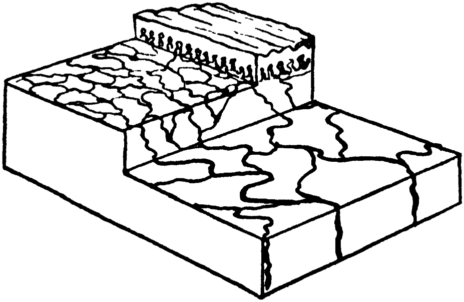

FIG. 9. Diagram of the skin, greatly magnified, cut in various planes to show two networks of blood vessels, from the upper of which capillary loops project towards the surface.

A small portion of the latter is represented by the ridged surface in the upper part of the diagram. (Simplified from Spalteholz, "Hand Atlas of Human Anatomy".)

The fundamental rate of heat production, which must be supplemented in the cold but which is not diminished in warm surroundings, represents the minimum activity which the various parts of the body must maintain to keep the body alive, and is known as the "basal metabolic rate" or B.M.R. As we said earlier, it is *about* 1800 kgm.-calories per day. It is not absolutely invariable because it is influenced by the activity of the thyroid and other ductless glands (Chap. XVIII), and also by the age and sex of the individual and the climate in which he lives. It will be noticed that these are not factors which produce or require *sudden* changes: they are responsible rather for "setting" the B.M.R. at its characteristic level.

We have now raised a large number of new questions. We know that those reactions we have described actually take place because they have been observed. They are matters of fact.

But we wish to know several things about them. For instance, how is it that the flow of blood through the skin can be increased and decreased? How is it that water can be poured out on to the surface of the body in such large quantities when we perspire? How does it come about that in the cold our muscles, which are normally quite under control, take the law into their own hands by shivering and begin to manufacture the heat which we need? Perhaps the most important question of all is: how does it come about that all the various devices are thrown into activity at the right moment? How does the body know when it is getting too hot or too cold, and what is the mechanism whereby heat production and heat loss are so balanced that each is proceeding at the same rate as the other?

We shall discuss this last question first, and postpone consideration of the others.

The control of temperature

To begin with it is necessary to realise two things. *First*, for the body temperature to remain constant, the rate of heat production and the rate of heat loss must be equal, but they can themselves be at any level. A resting man in equable surroundings is producing heat at a slow rate and losing it at the same slow rate. A man doing heavy work is creating a great deal of heat per minute but he is also losing the same amount per minute, and his temperature may be the same as that of the resting man. *Secondly*, equality in the rates of heat production and heat loss does not in itself guarantee any particular temperature. It guarantees only a constant temperature. We are, therefore, confronted by two separate facts: (1) that heat production and heat loss are accurately balanced one against the other at all levels and (2) that the temperature which this balancing process actually maintains is 37° C. The second fact must be accepted: we cannot explain it.

In an ordinary physical system constancy of temperature is achieved by means of an instrument known as a thermostat, so constructed that a sensitive element, perhaps a metal, switches on a heater when it shrinks as a result of cold and switches it off on expansion as a result of heat. It has been discovered that there is a "thermostat" in the body and we know approximately where it is. We do not know in absolute detail how it works, though we can fill in the gaps in our knowledge by intelligent guesswork and our guesses are not likely to be far from the truth. The thermostat is composed of nerve cells (see Chap. IV) in a certain part of the brain called the hypothalamus, and these cells are sensitive to two kinds of influence. The first of these is the temperature of the blood. When it rises or falls ever so slightly the activity of the nerve cells is modified. The second is the stream of nervous messages which come from parts of the skin exposed to the changing temperature of the environment. Although we shall not be able to visualise the working of this receiving mechanism until Chapter IV, there is no bar to our understanding it in a rough way on the basis of our own experience. When we touch a cold object with our hands we say it "feels cold". We do not worry about how the message has been conveyed to the "conscious" part of our brain, but there is no doubt that it gets there. The new fact we must appreciate is that messages also pass to some parts of the brain (e.g. the hypothalamus), of which we are quite unconscious. When they arrive they do not set up actual *sensation*, but they do cause nervous *activity*.

We may similarly draw upon experience to understand the transmitting side of the mechanism. When we wish our hand to move, it moves to precisely the spot where we will it to go. A message has passed from the "conscious" part of the brain to the muscles of the arm. The nerve cells which control the machinery for adjusting heat production and heat loss act in the same way, except that we do not *voluntarily* throw them into activity, and we are very often unconscious even of the results of the messages which they send out. These messages, whose purport is determined by "information received", go to structures like muscles, blood vessels and sweat glands which we already know to be important in regulating temperature. They take the place of mechanical movement in an ordinary thermostat.

It is usual to refer to a group of nerve cells which performs a receiving, co-ordinating and transmitting function of this kind as a " centre ". A great many of the activities of the body whose object is to keep it adjusted to its environment are under the control of centres (Chaps. IV and V).

A digression

We may use the knowledge we have already gained to illustrate a very common physiological principle. This is that most of the steadiness which an animal exhibits, in spite of fluctuations in its environment, is determined by the adjustment of the *rates at which processes take place*. Is is essential to regard the animal not as a static object but as a bundle of activities which, though never ceasing, never become unbalanced. The preservation of this equilibrium gives us the *appearance* of stability with which we are familiar, but it is a great mistake to suppose that we can understand or even appreciate it properly by imagining the whole machinery to be arrested at a particular instant, and setting out to describe it.

Any process out of step with its fellows leads, if not checked, to death. This is very easy to see in the regulation of temperature. The slightest excess of heat production over heat loss will lead inevitably to a steadily rising temperature. On the other hand, the body *can* work at a somewhat higher or lower temperature than the " normal ", so that small fluctuations do not matter provided they are within certain limits, and so long as a component of the mechanism does not get out of control (see fig. 12).

We should always try to gain an idea of the consequences of a certain degree of deviation from the normal. It will give us a sense of perspective to find what the consequences of a 10 per cent increase in the rate of heat production would be if it were unchecked. Suppose a man were producing 3300 kgm.-calories per day instead of 3000 and the additional 300 kgm.-calories were not balancd by an equivalent heat loss. Since a 70 kgm. man requires about 60 kgm.-calories to raise his temperature by 1°, his temperature would rise by about 5° in one day. Towards the end of the second day, he would die. These figures are in themselves relatively unimportant, but the impression they convey, namely, an idea of the seriousness of a 10 per cent difference, is very important. It is the equivalent in physiology of " road sense " in driving a motor car or the " feel " of a tool or instrument in any skilled occupation. It is typical of the unconscious standard of judgment which a doctor applies in his examination of a patient and which tells him whether the signs and symptoms which he finds are serious or not, and whether they require urgent treatment. With experience he has developed a sense of the rates at which processes occur in the body, and of how far and for how long they may deviate from the normal without permanently impairing the machinery.

CHAPTER III

COMFORT, CLOTHES AND CLIMATE

In the last chapter we discussed very briefly the temperature regulation of the unclothed individual so as to gain a clear idea of the principles involved. In everyday life in temperate and cold climates people always wear clothes, and this important complication must be taken into account. Only between 28°C. and 30°C. can the naked person control his temperature by means of adjustments in the skin circulation. Above this range he must perspire; below it he must move about. We may call the range of temperature between 28°C. and 30°C. the *comfort zone* in the absence of clothing. It is very small, but both mild muscular activity and clothes extend it materially. For instance, moderate exercise by the naked man prevents him from passively losing heat below 28°C., so that his comfort zone extends from about 18°C. to 30°C. This is easy to understand, though it must be remembered that in the higher part of this range if he keeps moving he will have to make use of vaporisation to a greater extent than before.

The alternative way of extending the comfort zone is by clothing. A lightly clothed man lying quite still and producing heat only at the basal rate can without difficulty maintain his temperature when exposed to 22°C. What is quite comfortable for one person may not be for another, and no hard and fast rules can be laid down for the amount of clothing which should be worn. Naturally the more there is the more comfortable a person will be at low temperatures, but the less comfortable he will be at high temperatures or during exercise.

Those who are familiar with the subject of physics will have noticed that we have so far referred only to radiation, convection and evaporation as means by which heat can be transferred from the body to the air and other objects, whereas it is well known that a warm body in contact with a cold one will lose heat by the process known as conduction. There is no point in going into abstruse details about what precisely conduction is. If the reader puts his hand on a bad conductor of heat, such as a blanket, he will experience practically no sensation of cold, whereas if he places it on a metal surface at the same temperature, it will be quite cold to the touch because it promptly removes heat from the skin. In the ordinary course of events our bodies are very little in contact with any object which can act in this way. Even when we sit down, only a relatively small part of the surface of the body is in indirect contact with the chair, and the chair is generally made of poor conductors of heat. It is much more likely to check the loss of heat by acting as a localised piece of clothing than to increase it by conducting heat away.

Conduction is the method of heat transfer *in* the body. Although it plays little part in heat loss *from* the skin surface, it is the way in which heat is transferred *to* the surface. The less readily the " outer layer " of the body conducts heat, the nearer is the outside surface to the temperature of the air, and therefore the less is the loss of heat to the surroundings by radiation, convection and evaporation. The rate of heat loss depends on both the temperature and area of the outer surface; the area can be reduced by curling up into a ball, or increased by lying with arms and legs extended. The basal metabolic rate of animals is proportional to their surface area, not to their weight (Table I). If clothes are worn, the surface of the

TABLE I

(From *Starling's Principles of Human Physiology,* Lovatt Evans, 1947.)

	Body weight, kgm.	Calories lost per square metre body surface per day
Animal 1	30.40	977
Animal 2	23.70	1069
Animal 3	19.20	1135
Animal 4	17.70	1040
Animal 5	10.90	1109
Animal 6	6.45	1054
Animal 7	3.10	1091

clothing becomes the outer surface of the body. Non-conducting clothes need not be heavy. Motionless air is a bad conductor of heat, and materials like knitted wool, which enclose countless little air pockets, are both warm and light. Unfortunately, they may be sufficiently porous to let in the wind and defeat their object, an increase in thickness of the poorly conducting layer, by allowing convection to take place. It is usual, therefore, to have a closely woven wind-resisting outer covering. Many layers of thin clothes are warmer than a single garment of the same total thickness, because between each pair is a layer of relatively still air. Animals achieve an extra covering by making their fur stand on end when it is cold, so trapping an additional thickness of air.

In very *warm surroundings*, whose temperature approaches that of the skin, radiation is no longer effective, because a body cannot radiate heat to one equally warm. Similarly convection cannot take place. Cooling therefore depends on vaporisation, and as this still occurs at the *skin* surface, the outside of the clothes may then be warmer than the skin. In very hot climates, the disadvantage of clothes in checking the movement of air (which assists evaporation) may be offset by their protecting the body from the radiant heat of the sun and surrounding objects. Thus the Arab in the arid desert reaches a very satisfactory compromise with nature by means of his burnous. The air is so dry that evaporation takes place readily enough through its folds, while its surface, particularly if white, shields him from the sun. At night it affords him protection from the bitter cold. The South Sea Islander, on the other hand, lives in a moist warm climate. In the humid air, clothes would make it more difficult for him to sweat. Moreover, he probably has a plentiful supply of water to drink, and need not fear dehydration through perspiring too freely. He can thus keep his temperature down in spite of radiant heat from his surroundings, and wears little or no clothing.

It is in virtue of perspiration that man can live in surroundings hotter than the body, though humidity, for instance, near tropical swamps, reduces the extreme of temperature which he can support. If the atmosphere is quite saturated with moisture he can scarcely lose heat by evaporation at all,[1] and between 90° and 95°C he will become unable to stabilise his body temperature. On the other hand, two enthusiastic investigators in 1775 stayed for a quarter of an hour in a *dry* room heated to 120°C in which beefsteaks were being cooked by the heat of the air. Their own temperatures did not rise.

TABLE II.

(Adapted from Bedford, *J. Inst. Heatg. and Ventilg. Engineers,* November 1936)

Air temperature °F.	Number of observations	Percentage of persons who felt really comfortable	Percentage of persons who felt definitely uncomfortable
54 to 55.9	13	46	40
56 to 57.9	87	49	23
58 to 59.9	131	53	22
60 to 61.9	395	75	13
62 to 63.9	608	83	12
64 to 65 9	399	79	7
66 to 67.9	417	71	12
68 to 69.9	349	57	13
70 to 71.9	141	41	18
72 and over	31	45	39

It can now readily be appreciated how important are atmospheric conditions in factories and other places where people have to work and therefore produce heat of their own, and why factors like air movement and humidity have to be taken into account as well as mere temperature.

In ordinary living rooms or offices, where people are neither crowded together nor doing physical work, loss of heat by sweating and therefore atmospheric humidity are for the most part unimportant in a temperate climate, though we are all familiar with the discomfort of hot damp days. Given good ventilation and a suitable heating system, indoor comfort depends principally on temperature. But it also depends on the individual, his clothing, and his habits. Table II shows the result of asking a number of people if they were comfortable at various temperatures. The most obvious fact is that most of them were comfortable over quite a wide range. Equally striking, however, is the fact that at no temperature were they *all* comfortable.

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[1] If the air temperature is less than the skin temperature he can evaporate some sweat, because the layer of air next to the skin becomes heated by the skin and is then capable of taking up a little more moisture.

When ventilation is inadequate, a room feels " stuffy ". This is due to a variety of causes, such as lack of air movement, but the chief is excessive humidity, a result of the evaporation of moisture from the skins of the people in the room. It will be recalled that even at temperatures at which sweating is in abeyance, a certain amount of vaporisation occurs, and in the aggregate it can exert a considerable influence on the air. A room also tends to feel uncomfortable if the walls are colder than the air, or if the air at the top is hot and that near the floor is cold. Heating and ventilating systems should avoid these faults, and provide sufficient air movement without draughts.

Fever

Another practical point which we must mention is the change which sometimes takes place in the temperature of the body itself. It will be clear from what we have said that, in taking this temperature, methods must be devised in which the recording instrument is not subject to the vicissitudes which influence the temperature of the skin. There are three common ways of achieving this object. They are to place the thermometer (fig.10) or recording device in the armpit (with the

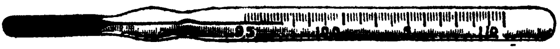

FIG. 10. Diagram of clinical thermometer.

Instead of the column of mercury being withdrawn into the bulb when the thermometer is cooled, the kink causes it to break, so that the part farthest from the bulb remains in position and records the highest temperature to which it has been exposed.

arm pressed to the side), in the mouth, or in the rectum. The last method is scientifically the most satisfactory, but practically the least convenient. It yields a temperature somewhat higher than the other two methods. So long as this difference is borne in mind the simpler methods are quite satisfactory if precautions are taken to ensure that the bulb of the thermometer is not exposed to the air. In the mouth it should be placed under the tongue and in the armpit it should be completely enclosed by skin.

Preliminary examination of the normal resting person reveals that his temperature is by no means absolutely constant, but fluctuates regularly throughout a small range (fig. 11). The time of day must therefore be taken into account in deciding whether a rise in the temperature of the body has taken place and if so how large it is. Fig. 12 shows another source of error, namely, that temperature also depends on the activity of the subject. It used to be thought that the rise, amounting to as much as 2° or 3°, which takes place during muscular exercise, was due to temporary embarrassment of the heat-losing mechanisms, but more recent researches suggest very strongly that this idea is incorrect and that the raised temperature is a normal accompaniment of exercise. The temperature is, as it were, deliberately " set " at the higher level. Another situation in which body temperature may be at a higher level than normal is when the external temperature is approaching the limit of endurance. The resulting rise of body temperature may enable just enough additional heat to be lost to stabilise it.

In sickness, the temperature of the body frequently rises, and this is due to a disturbance of the temperature regulating centre in the brain. It becomes " set " at a higher level, but also seems to become more unstable, so that a very high temperature in the evening may be followed by an almost normal temperature the next morning (fig. 13). This is by no means a rule, and different infectious diseases have fairly characteristic temperature charts. A day-to-day record furnishes a valuable index to the progress of a febrile disease, particularly if it is one which habitually follows a well-established temperature course. It is a matter of dispute whether a high

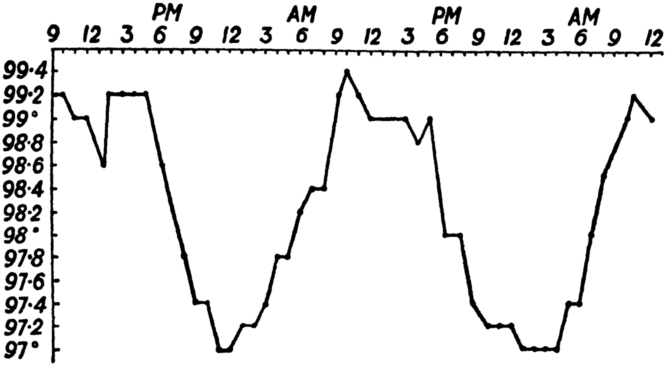

FIG. 11. The daily fluctuation in temperature of a healthy person. Somewhat different ranges may be covered by different individuals.

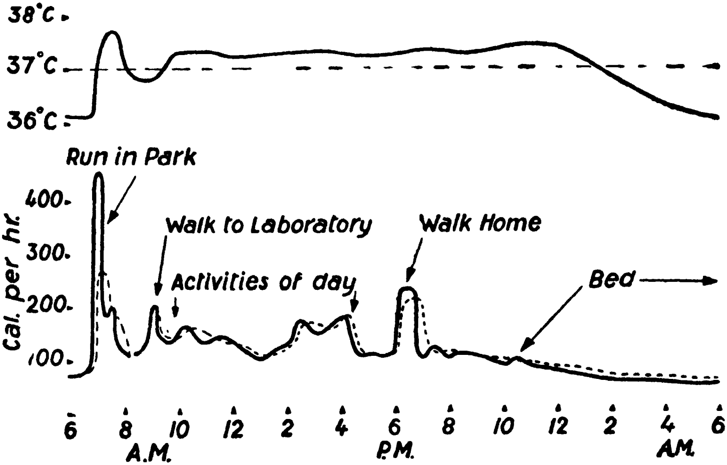

FIG. 12. The top curve shows the fluctuations in temperature which actually occurred in a normal individual during the 24 hours. These are explained by the lower half of the figure in which the solid line represents the rate of heat production and the dotted line the rate of heat loss. It will be noticed that they do not coincide and in particular that there was a steady loss of heat during the night. (Du Bois, Harvey Lectures, 1938–39.)

temperature has a beneficial influence on those processes which are fighting the disease, but it often produces considerable discomfort. For this reason drugs (for instance, aspirin) may be administered to keep the temperature down, and they appear to re-set the temperature regulating centre at the normal level. Although it is generally easy to bring a high temperature down, it is difficult to make a normal temperature lower. For reasons which are not understood, drugs seem only to influence the temperature regulating centre when it is disturbed.

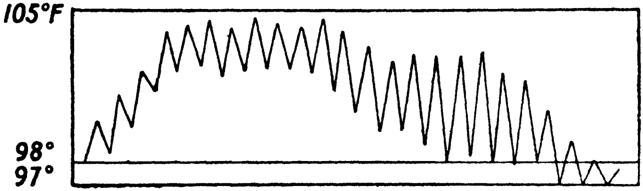

FIG. 13. Successive morning (troughs) and evening (peaks) temperatures in a case of typhoid fever.

There are one or two diseases in which the responsible organism is known to be killed by a temperature slightly lower than that which kills the human body, and the condition may be sufficiently serious to warrant the actual heating up of the patient by artificial means to an unusually high degree. This naturally has to be done with extreme care, and allowance has to be made for the fact that when the body is so heated, and the temperature regulating mechanisms overborne, oxidation is accelerated so that the body itself is producing more heat than it was.

In considering the limits to which body temperature can rise without fatal results, we encounter the variation between individuals which we have mentioned before. Some people undoubtedly succumb to lower temperatures than others, and, conversely, " record " temperatures have been observed which have been followed by recovery though they would have been fatal to the majority of persons. Such temperatures usually lie between 108–110°F., but few people can survive a body temperature of over 107°F.

Heat stroke is the collapse which occurs when a man is exposed to excessive heat or tries to do physical work under environmental conditions which forbid the loss of heat. It is accompanied by a raised temperature, which must be brought down quickly by cold applications because of its accelerating effect on oxidative processes and the danger of a vicious circle being created. In most cases of heat stroke the individual has been exposed to hot climatic conditions for some time and may have been adapting himself successfully when suddenly the sweating mechanism fails, and his temperature rises. The mechanism generally rights itself when the body temperature is brought down and kept down for a few days.

Other victims do not succumb suddenly in this way, but the strain tells upon some other part of the system, for instance, the heart and circulation. In a hot dry climate a man may lose about 10 pints of sweat in a day and this represents water he has drunk. It all has to be transported in the blood which is pushed round by the heart (Chap. VIII). In cases like this a condition known as heat exhaustion may take place, and be complicated by the fact that the sweat contains a certain percentage of salt. Excessive sweating may lead to a serious loss of this important mineral.

Subnormal temperatures are not often met with, but may result from prolonged inanition or from shock, and occasionally from diseases in which destructive processes involve ductless glands or parts of the brain. Higher temperatures may also occasionally result from the last-named causes.

CHAPTER IV

CENTRES OF CONTROL

1. THE MECHANISM OF NERVOUS ACTIVITY

So far we have avoided technical details about the structure of the body and have managed very well by taking for granted, for instance, that muscles are responsible for movement. We have not yet discussed the structure or precise mode of action of a muscle. In the same way we have mentioned blood vessels, but again we have not had to go very far outside ordinary everyday experience. We can see the veins of our arms, we can feel the pulsation of the various arteries, and it is common knowledge that blood is circulating in these tubes. This has so far been quite sufficient for our purposes. Now, however, that we have decided to study the central control of the body, we must embark upon a more detailed explanation about nerves and nerve tissues in general. These are not accessible to direct inspection, since they do not bulge like a contracting muscle or pulsate like arteries with a flow of blood.

The *central* nervous system consists of the brain (including the brain stem) and the spinal cord (fig. 30). The brain is enclosed in the skull (fig. 14*A*) and the spinal cord in the *spinal column* (fig. 15) which consists of *vertebrae*, made of bone like the skull and placed one upon the other up the middle of the back. These separate bones can be felt beneath the skin. In each one of them is a hole (fig. 14*B*), and the holes, being superimposed upon each other, form a continuous tubular cavity in which the spinal cord is suspended. The bones are joined together by tough but flexible strands known as ligaments, so that they cannot slip out of position, though a certain degree of sliding and twisting of each bone upon the next is possible. This accounts for the fact that we can bend forwards and backwards and twist round. If the back of a person undergoing these movements is inspected, it will be

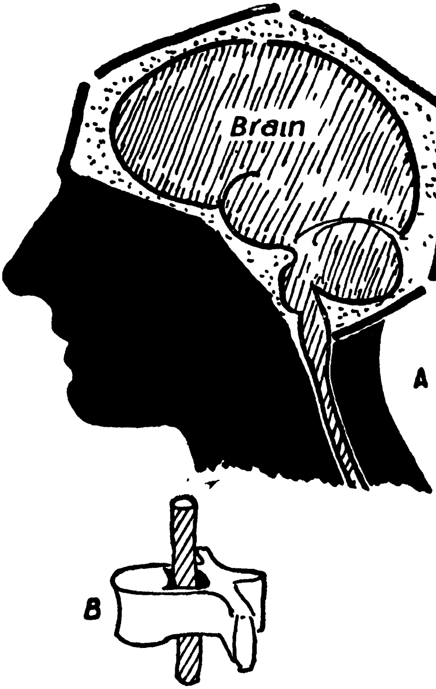

FIG. 14. The protection of the central nervous system.

A. The position of the brain in the skull surrounded by suspending and protective structures which are indicated by stippling. The beginning of the spinal cord is also shown.

B. The spinal cord passing through one of the vertebrae in which it is similarly suspended and protected.

immediately seen that the greatest bending represents the sum of only small displacements at each intervertebral joint, of which there are 24.

During movement of the spine, at no point is the soft spinal cord kinked or distorted. At the most the cord assumes only gentle curvature which does not interfere in any way with its working. To make it more secure from injury, it is suspended from its bony case by a network of fine fibres which run in a watery medium known as the *cerebrospinal fluid*. We have, therefore, going from without inwards, first of all the bony case, then a layer of fluid and finally the spinal cord suspended in its midst. The brain is similarly suspended within the skull, but it is quite obvious that the skull always moves as a whole, so there is no question of parts of the brain moving in relation to each other. The protection of the brain is, therefore, purely a matter of adequate covering and reasonable immunity from direct blows and jerks, and we may take it for granted that such protection is afforded.

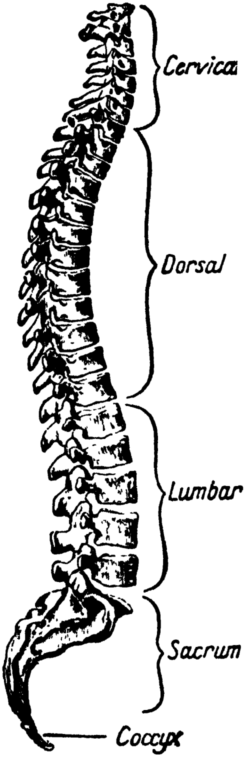

FIG. 15. The complete spinal column seen from the side showing its natural curvatures.

What interests us most at present is the *internal* structure of the central nervous system. This becomes very complicated as the higher and most important parts of the brain are approached, where its working is not fully understood. The lower parts of the brain and the spinal cord are, however, much easier to understand and their function can be correlated with their structure. Let us take the spinal cord first. A cross-section of it is sketched in fig. 16. In an actual cord the central part which, as we see from the figure, is somewhat H-shaped, is grey in colour, and the outer part is whitish. The outer white part is composed entirely of ***nerve fibres*** running longitudinally up and down the length of the cord, and ultimately in and out of the brain.

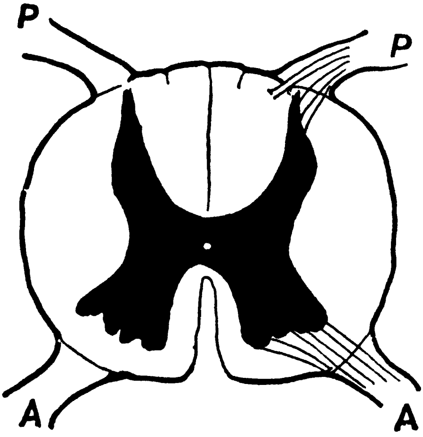

FIG. 16. Cross-section of the spinal cord at a level where the posterior (P) and anterior (A) nerve roots emerge.

The term *fibre* in physiology is purely descriptive and the different kinds of fibre which are found (fig. 17) are qualified by adjectives to indicate their function. Thus we have *muscle fibres*, which as their name implies are the chief components of muscle, and have the power of forcibly shortening themselves and pulling together the structures to which they are attached at each end. We also have ***collagen connective tissue fibres*** which have no power of contraction and are so inelastic that they resist stretching; we find these in structures like tendons, which can readily be felt at the wrist, and which merely serve to connect the ends of muscles to some remote point which the muscle moves from a distance, e.g. the fingers. Then there are ***elastic connective tissue fibres*** which, although incapable of contracting like a muscle, can nevertheless be passively stretched and which return to their original length

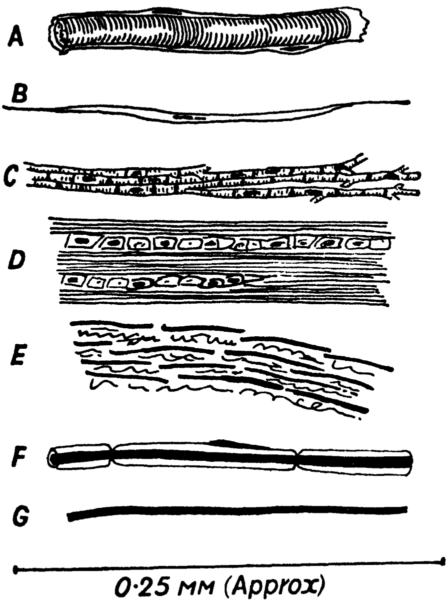

FIG. 17. Kinds of fibre encountered in the body showing very approximately their relative sizes.

A. Part of *voluntary cross-striated muscle fibre*. This is under the control of the will enabling us to move limbs, etc. The complete length of the fibre may be five hundred times its diameter. It is enclosed in a transparent membrane.

B. *Involuntary smooth muscle fibre*. Not under the control of the will and responsible for movements of the alimentary tract and other internal organs. It controls the diameter of blood vessels.

C. *Heart muscle fibres*. Not under the control of the will. Cross striated fibres which branch, unlike the other two varieties.

Fibres A, B and C are all true living cells of an elongated shape.

D. *Collagen fibres of tendon*. These are not living cells though they have been manufactured by them. They are flexible but inextensible. Rows of cells which have no mechanical function are seen embedded in the fibres to which they are probably necessary for purposes of maintenance.

E. *Thick elastic fibres*. These run circularly in the wall of a very large artery and allow it to be stretched. Between them, and drawn much thicker than they really are, lie very fine coiled collagen fibres which straighten out when the vessel is distended and check its expansion. Smooth muscle when the tension is released. They are found in the walls of large blood vessels, which very often have to " give " a little to accommodate blood which is forced into them, but which assume their former size when the pressure dies down. Both elastic and inelastic connective tissue fibres are found in the ligaments which maintain bones in contact with each other. They allow movement at the joints while preventing the bones from becoming separated. A very delicate type of connective tissue fibre is found in the soft parts of the body in the form of a fine feltwork, which supports delicate structures. Finally, we have *nerve fibres* whose function is neither contraction nor support, but simply the conduction of excitation.

Excitability is a fundamental property of all living matter and even the humblest organisms generally move when touched. In higher animals muscle fibres will do this, though a more convenient stimulus is a small electric shock. Muscle, therefore, exhibits both the power of movement and the property of excitability, but connective tissue fibres possess neither of these properties. Nerve fibres are unable to move, but they show the phenomenon of excitability in a high degree, and they also conduct the excitation very rapidly along their length. If they did not do this we should know very little about their excitability, because they show no *visible* sign of it, such as movement. However, the transmission of the excitation enables it to be detected in other ways and to stimulate other structures whose activity is obvious. For instance, on receiving excitation from nerves, muscles contract and glands pour out chemical substances. Sometimes the structure excited by a nerve fibre is not a muscle or gland but another nerve fibre, which in its turn transmits excitation.

Protoplasm is a name for the substance of which all the active parts of the body are made. *A cell* is a collection of protoplasm which can be recognised as a unit; that is to say, which is divided off from its fellows by a surface of some kind, recognisable microscopically. Different kinds of cells have different kinds of protoplasm; thus, muscle protoplasm is chemically different from nerve protoplasm, but all kinds contain a very high proportion of water

and other cells are present but are not shown. In delicate supporting tissue extremely fine elastic and collagen fibres are found. Both kinds of fibre, like those of tendon, have been laid down by cells but are not themselves cells, and are capable of only passive movement.

F. *A nerve fibre* (black) surrounded by its fatty sheath (white). The whole is enclosed in a transparent membrane like that of the voluntary muscle fibre.

G. *A smaller and unsheathed nerve fibre.* All nerve fibres are parts of cells (neurones) and if separated from the parent mass of protoplasm containing the nucleus, they die.

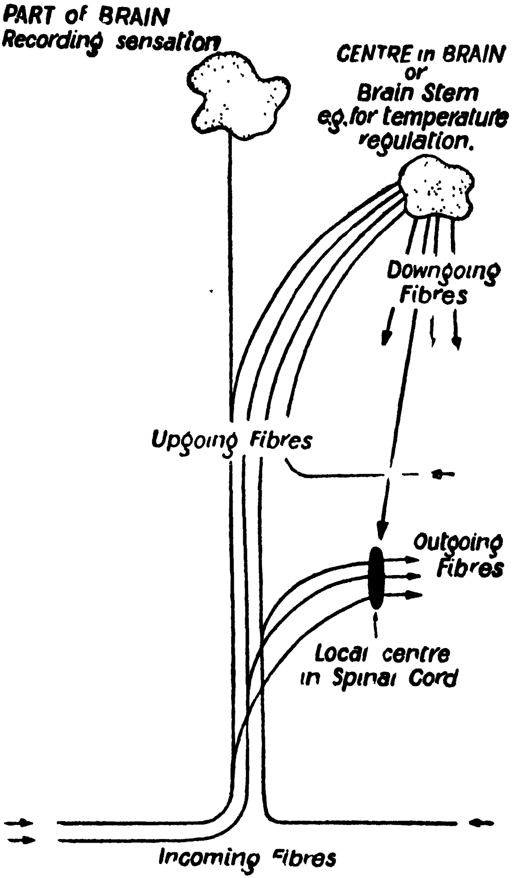

FIG. 18. To show the significance of the conducting paths in the spinal cord. This is a purely diagrammatic sketch.

and are in the form of a jelly. We have already said that some cells are able to manufacture chemical substances, and it is interesting to note that the more solid tissues, like bone and connective tissue, are made of substances which the protoplasm of special types of cell has produced.

Somewhere in the protoplasm of a cell a spot of a perceptibly different kind of protoplasm is embedded, and this is known as the *nucleus*.

The fibres passing *up* the cord enter the brain where they are distributed to various centres, whose task it is to relay an ordered pattern of excitation. The nerve fibres passing *down* the spinal cord generally transmit the excitation from the brain to other nerve fibres, which then leave the cord and stimulate outside structures like muscles and glands. They may maintain some co-ordinated and possibly quite complicated function, like the regulation of temperature (fig. 18). All kinds of structures may be thrown into activity simultaneously, that activity being, moreover, very finely graded.

Other fibres going to the brain excite certain nervous elements there whose activity is associated with *sensation*. Although we know the destination of such fibres in the brain, we do not know why the activity of particular parts of it should be conscious while the activity of other parts is quite unconscious. Most of the sensation which is provoked by nerve fibres passing up the spinal cord originates in the skin and muscles. The organs of sight, hearing, taste and smell, the *special senses*, are connected directly to the brain above the level of the spinal cord (fig. 33). In addition to causing sensation all these special sense fibres activate " unconscious " nervous centres just as do other sources of excitation.

Although the longitudinal conducting paths of the spinal cord indicate by their bulk the importance of communication between the higher and lower parts of the central nervous system, a great deal of excitation is dealt with locally in the cord itself. We have described the out-going fibres (they are in the anterior nerve roots, fig. 16) as recipients of excitation from the brain, but they are also copiously excited by messages coming into the cord in their own vicinity and carried by fibres belonging to the neighbouring posterior nerve roots which terminate locally. Actions of muscles (and as we shall see of other organs) caused by nerve fibres which have been excited locally are usually called *spinal reflex actions*, or just *spinal reflexes* (fig. 42). The cord is not only an important "up and down" arterial road, but is an unimaginably intricate relay station for "transverse" paths.

Nerve cells

If we follow a nerve fibre from its end we ultimately come to a point where it suddenly balloons out into a mass of protoplasm. This is the "body" of the nerve cell (fig. 19) to which that fibre belongs, and it contains a nucleus. The nucleus is important because, even though a nerve fibre may be several inches long and one might think that the protoplasm in it was sufficiently far from the cell body to be independent, nevertheless, if severed from that part of the protoplasm which contains the nucleus, it dies. The nerve fibre is different from a connective tissue fibre in that the latter is merely a *product* of cellular activity while the former is actually *part* of the cell itself. For the sake of completeness we may remark, at this point, that the muscle fibre is also a cell containing a nucleus, and although the nucleus may be pushed very much to one side, no part of the fibre lives independently without it.

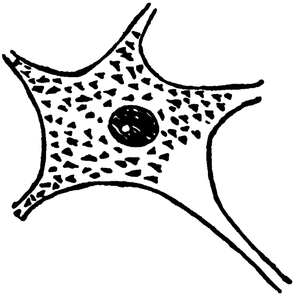

FIG. 19. A nerve cell drawn to a comparable scale with the fibres of Fig. 17.

It is incomplete because only the beginnings of the fibres which belong to it are shown. The specks in the protoplasm are called Nissl's granules and occupy all parts of it except the projection which gives rise to the nerve fibre carrying impulses out from the cell. Only one fibre does this. The rest collect excitation from sense organs or other neurones according to the location of the cell.

The cell bodies of the long fibres which pass *down* the spinal cord lie in various parts of the brain, and are generally components of the nervous centres which we have mentioned. The cell bodies of the nerve fibres which pass up the spinal cord lie either just outside the cord in collections known as *spinal root ganglia* (fig. 31) or in the central grey part of the cord, where they are supported by a delicate connective tissue feltwork known as *neuroglia*.

The anatomical situation of the bodies of nerve cells is important for two reasons. In injury or disease of a certain part of the nervous system it determines where the dead fibre will be found. Thus, if the connection of one of the spinal ganglia with the cord is severed, then the dead fibres will be found in the spinal cord itself, whereas if the bundle of fibres leaving the ganglion in a direction away from the spinal cord is severed, the degeneration will occur outwards and the fibres in the cord will be largely unaffected (sometimes, however, a whole cell with all its fibres will die as a result of injury). We are not very much concerned with the question of injury. The position of cell bodies is important to us for a second reason, namely that collections of nerve cells occur to which definite functions can be assigned, and it may be important to know exactly where these " headquarters " lie (see Chap. V). Nerve cells, however, have a very important physiological significance which we must study before referring to their actual positions.

Transmission of excitation within the neurone

A complete nerve cell with its cell body and all its fibres is called a *neurone*. It is clearly possible to have a great many shapes and sizes of neurone and we must forego description of all the different kinds which exist and concentrate on understanding how they work. So far as we know, the basis of co-ordination is the same throughout the nervous system and we may conveniently describe this by means of simplified diagrams. In fig. 20*A* the three essential parts of a neurone are shown diagrammatically; the fibre (*a*) conveying excitation towards the cell body, the cell body itself (*b*) and the fibre (*c*) taking excitation away from the cell body. The latter fibre is called the axon. Fig. 20 also shows the relation which the different parts of the nerve cell may bear to the central nervous system. In fig. 20*B* typical neurones (*n*) are drawn which convey excitation from the receptor organs in various parts of the body to the central nervous system. The cell bodies lie just outside the spinal cord. Fig. 20*C* shows a neurone which lies entirely within the central nervous system and which may transmit excitation from a low level to a high level. Fig. 20*D* shows a neurone also lying completely within the central nervous system which transmits excitation in the opposite direction and *E* shows a typical neurone conveying excitation

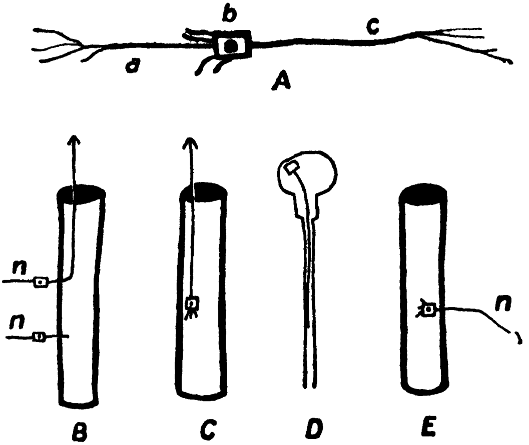

Fig. 20. A. The essential parts of a neurone.

(*a*) The collecting fibre or dendrite.
(*b*) The cell body.
(*c*) The transmitting fibre or axon.

There may be more than one dendrite.
B, C, D and E. Typical situations for neurones in the central nervous system. The tubular outlines of B, C and E represent pieces of spinal cord. The more complicated outline of D, drawn to a smaller scale, represents, from above downwards, the brain, brain stem and spinal cord, i.e., the whole central nervous system. For explanation see text.

from the spinal cord to some organ like a muscle whose activity is to be controlled.

Those parts of the neurone in fig. 20*B* and *E* which are labelled *n* are collected together shortly after they leave the central nervous system into bundles, and constitute what we know as nerves. A single nerve fibre is too small to be seen except under a microscope, but a sufficiently large number of them collected together are easily visible and some of the nerve trunks of the body are quite large. If the arm is straightened and the region of the elbow explored with the finger, a nerve can be felt running in the hollow which lies between the big bony point of the elbow and a small bony projection on the inside. It feels about the thickness of a picture cord and if manipulated too vigorously will give rise to an unpleasant sensation. These big trunks branch again and again as they approach their destinations, and some of the small branches are often referred to as nerve twigs. A nerve like that which can be felt at the elbow may contain tens of thousands of fibres.

We must now try to gain a picture of what we have so far called excitation. In the body, a neurone is never excited *naturally* in any part of its course *except at one end*. The sensation we get by pressing the nerve running behind the elbow is quite abnormal, although it shows that the fibres have been thrown into activity. For reasons we shall appreciate in a moment, the analysis of excitation cannot be completely carried out by studying a nerve excited through the normal channels, and advantage is taken of the fact that *mechanical*

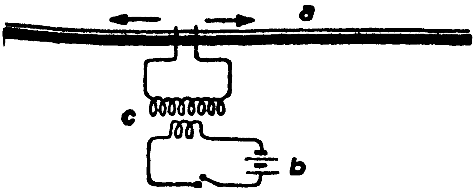

FIG. 21. Excitation of nerve (*a*) by a battery (*b*) and an induction coil (*c*).

✓*Or electrical disturbance at any point of a nerve fibre will stimulate it.* When a nerve is removed from the body and kept alive, it is found that a single electrical shock at any point (fig. 21) will give rise to a transient disturbance which runs in both directions from the point of stimulus along all the fibres of which the nerve is composed, irrespective of whether they were originally running towards or away from the central nervous system. This transient disturbance, which is called a *nerve impulse*, can be detected because it is accompanied by an electrical potential.

✓It is common knowledge that negative particles of electricity or electrons form parts of the atoms and molecules of which all matter is ultimately constituted, and that the structure of atoms and molecules is such that these are electrically neutral. This state of affairs exists in a resting nerve fibre and in almost any other object we handle.

If we cut any object in two with a knife then the two halves are still electrically neutral, as are any further subdivisions we make, but by more subtle treatment a kind of division can be effected which cannot be seen visually but which is of a much more fundamental kind, because it forces the system into two parts, one of which has an excess of electrons and the other a deficiency. The former is conventionally called electro-negative and the latter electro-positive. There is a great tendency for equilibrium or *electrical neutrality* to be restored, and this is made use of extensively by providing an easy electrical path, for instance, a piece of copper wire, connecting the electro-negative and electro-positive sides of the system. The excess electrons on the electro-negative side stream along the wire back to the electro-positive side, and as fast as the mechanism (which we have not described) is forcing the original components of the system apart, the latter is trying to revert to its original condition by means of the wire pathway. We are all familiar with the advantages of this arrangement. It enables us to interpose various devices such as lamps, motors, etc., in the course of the wire, so making the stream of electrons, which we know as an electric current, do work for us. If we do not connect the two parts of the system by a wire, then the electrons have no easy path of return and so up to a point they accumulate, until the direct attraction between the electro-negative and electro-positive elements of the system is so great that the separating mechanism can do no more than just hold them apart. It can no longer make the electro-negative side any more electro-negative or the electro-positive side any more electro-positive.

The force with which the two sides tend to rejoin (which is now equal to the force exerted by the dividing mechanism) is called the *electrical potential* of the system.

✓When an isolated nerve is stimulated in its course, either mechanically by a tap or by a small electric shock, some internal disturbance takes place at the point of stimulation and we find that the outside of the fibre becomes more electrically negative than it was originally, and the inside to an equal degree more electrically positive. There is evidently a momentary excess of electrons on the outside of the fibres at that point (fig. 22*A*). The original condition is almost immediately restored because whatever disturbance caused the division dies away. But in the meantime the potential which has momentarily been created has acted as a mild electric shock to the adjacent bits of nerve, where similar disturbance is set up with a similar result. Just as the combustion taking place at one point in a train of gunpowder initiates combustion in the adjacent parts and leads to transmission of the ignition all along the train, so is the disturbance in a nerve fibre transmitted (fig. 22*B*), the difference being that the nerve fibre promptly returns to its original state and is ready to do the same thing again. If we place an instrument which is able to detect electrical potentials on a nerve, it will record the passage of

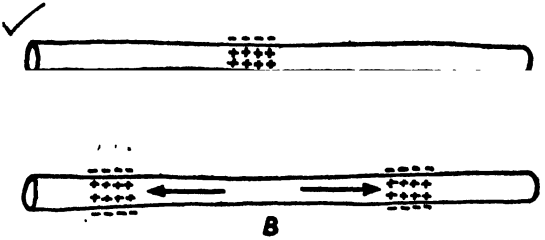

FIG. 22. Mechanism of excitation in a single fibre.

A. The initial disturbance of electrical equilibrium at the point of stimulus (the stimulus need not itself be electrical).

B. The passage of the electrical disturbance in both directions from the point of stimulation. *In the body*, fibres are never stimulated except at one end. Therefore conduction is always in one direction only.

the nerve impulse. It is important to realise that what passes along the nerve is not an electric current (which travels much faster) but some internal molecular convulsion accompanied by a purely local potential which appears and disappears at each point in turn. The energy which is used in forcing electro-positive and electro-negative elements apart in the nerve is supplied ultimately by means of the unknown local process. It must be oxidative, because nerve fibres can be shown to use more oxygen when they are working than when they are resting, but the quantities are very small and the exact nature of the process has not been elucidated.

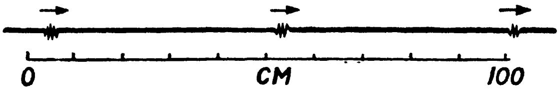

FIG. 23. Nerve fibres in action.

Impulses in large nerve fibres may travel as fast as 75 metres a second. Their frequency rarely exceeds 100 per second. If the impulses were visible, a fibre, carrying 120 per second at 60 m.p.s. and of 0.5 millisecond duration at any point, would appear somewhat as in the figure. As there are very few fibres in the body as long as one metre, there will rarely be more than a couple of impulses in a given fibre at any moment; and in a short fibre conducting even at a high frequency, there will be intervals when it is carrying no impulse.

Fine unsheathed nerve fibres conduct more slowly, often at one metre a second or less. If the metre scale shown above represented only one-third of a metre, then the nerve diagram would represent a thin fibre carrying impulses of 10 milliseconds duration at 1 metre a second and a frequency of about 6 per second (the scale refers only to length, not to thickness).

Impulses can follow each other along a nerve at very close intervals, and some fibres *can be made* to take more than 1000 a second. If, however, a second stimulus is thrown in *too* rapidly after the first it is found that the nerve is incapable of responding. In the body very few fibres have to take more than 120 impulses per second, which gives a sufficient interval between impulses for complete recovery (fig. 23). Very large nerve fibres can take more frequent impulses than very small ones and we find all kinds in the body. The impulse also passes much more slowly along a small fibre than along a large one.

The natural origin of excitation in neurones

Sense organs in the skin (fig. 103), and practically all other parts of the body, have the power when stimulated of initiating impulses in the nerves to which they belong. But the natural stimulus, e.g. touch, heat, cold,[1] is a very prolonged affair compared with the instantaneous electric shock which we use artificially to initiate and study single nerve impulses. Consequently, it gives rise to a *succession* of impulses at a frequency which depends on its intensity (fig. 24). Each individual impulse in any one fibre is the same as all its fellows. Only the *frequency* of impulses can vary in any one fibre. The velocity of the impulses in any one fibre is also always the same, but the fact that different fibres conduct at different velocities can be demonstrated quite easily. If we put our hand into very hot water and withdraw it immediately, it is quite evident that we feel the sensation of *heat* slightly before we feel *pain* of a rather unpleasant character. Very often the latter does not occur until we have actually removed our hand from the water. This is because the end organs in the skin which are specialised for responding to changes in temperature are connected with bigger and faster-conducting fibres than those which respond to painful stimuli, of which excessive heat is one.

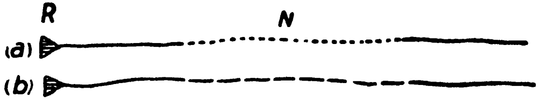

FIG. 24. The effect of strong (*a*) and weak (*b*) stimuli of equal duration applied for the same length of time to the receptor organ (R) of a nerve fibre (N). The frequency of impulses is indicated by gaps in the nerve fibre.

From Fig. 23 it will be seen that though this is a convenient way of indicating frequencies in diagrams, it does not literally represent the true state of affairs because the impulses could not be so near together.

If we take almost any stimulus, it is obvious that there is a place at which it is most intense and an "edge" where it fades off into no stimulus at all. The sense organs, for instance in the skin, which underly the centre of stimulation will discharge at a greater frequency than those around the edge, and there will be intermediate rates of discharge in intermediate fibres (fig. 25). With this difference in frequency and the difference in velocity of conduction between individual fibres, it can well be imagined what a medley of impulses is crowding into the central nervous system at any moment.

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[1] The reader from now on should not confuse the terms "stimulus" and "impulse".

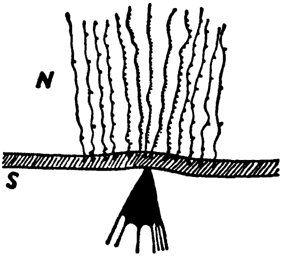

FIG. 25. The effect of deforming the skin (S) by pressure with a pencil point.

The frequencies of impulses in nerve fibres (N) belonging to receptors in the neighbourhood are indicated by dots.

This is a convenient point at which to state that we do not know exactly how a sense organ stimulates a nerve fibre. When we give a nerve an electric shock or tap it, we do at least know that these stimuli act upon it *directly* even if we do not quite understand the steps by which the disturbance is translated into an impulse. In the case of an end organ we are one step further back, because end organs are specialised to receive a particular type of stimulus such as pressure (fig. 26) or warmth or light or sound, and in some way the activity

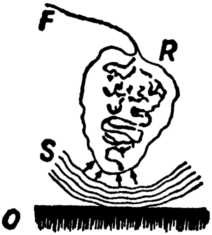

FIG. 26. Deformity of skin (S) produced by touching object (O) and giving rise to excitation in a receptor organ (R) and impulses in its fibre (F).

which this sets up in the end organ is further converted into nerve impulses. It seems as if whatever goes on in the end organ " builds up " a disturbance in the nerve fibre until it becomes large enough to achieve the creation of a full-sized impulse. Then the process is repeated. It seems that a weakly stimulated sense organ is incapable of building up this disturbance so rapidly as a strongly stimulated one, so that frequent impulses follow a strong stimulus and infrequent impulses follow a weak stimulus. As it is important for us to grasp this idea even though we cannot supply the details, we may resort to a mechanical analogy. The end organ may be likened to a cistern which fills up and then suddenly empties itself when the water, representing excitation, reaches a certain height; the sudden outflow of water represents the nerve impulse. The cistern then starts to fill up again, and the frequency with which it repeats the process depends on how hard the tap is running which supplies it. We can represent a weak stimulus by a slowly-running and a strong stimulus by a swiftly-running tap (fig. 27).

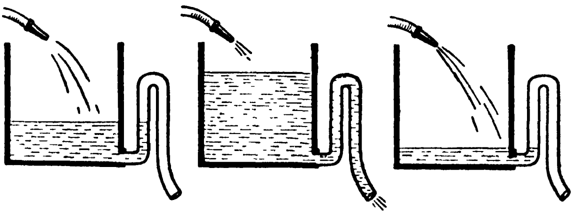

FIG. 27. The mode of initiation of nerve impulses.

The cistern represents the receptor organ; the water, excitation; and the pipe leading from it, the nerve. For explanation see text. When the level of water rises above the bend in the outflow pipe, the latter automatically empties the cistern.

In the body impulses are streaming down fibres whose duty it is to convey excitation *away* from the central nervous system, and we shall shortly consider their origin. Meanwhile let us think of their destination. This is either another neurone or an *effector organ*. In other words, an organ which does something. The most common are muscles and glands. The function of muscles is to contract, and the more nerve impulses which flow into it per second, the more it shortens. The function of a gland is to manufacture chemical substances and the harder it is stimulated the faster these are produced. We may note in parenthesis that the *building up* of a store of chemicals in the cell may be under an independent control, so that the impulses we are considering may have the effect of exhausting the gland of its supplies. The response of a muscle is much easier to measure than the response of a gland, and the response of those muscles attached to the skeleton which we can move voluntarily is much more precise than those of the internal organs which move involuntarily. The degree of shortening (usually measured as tension) of a "voluntary" muscle is extensively used as an index of the intensity of excitation of the motor nerve which supplies it (fig. 40).

The transfer of excitation from one neurone to another

An important requirement for the successful co-ordination of nervous activity is the transmission of excitation from one neurone to another. We have seen the origin of the grading of frequencies in fibres passing into the central nervous system, and the effects of grading in fibres passing out, but we have yet to gain an insight into what happens *within* the central nervous system, where contact is made between ingoing, outgoing and internally communicating neurones. A great deal must depend on the properties of the junctions or *synapses* between neurones.

It is incorrect to regard any single impulse as jumping the gap and continuing its independent existence in the second neurone. What happens may be visualised by resorting again to our comparison with a cistern (fig. 28*A*). This time the cistern represents the second neurone and the taps which fill it may be pictured as dripping at various frequencies. Each drop represents a nerve impulse passing down a preceding neurone. It will be noticed that we speak of many taps and not of a single one. This is because a neurone receives impulses from numbers of other neurones, and the speed with which its excitation is built up depends upon the *total* number of impulses reaching it, just as the speed at which the cistern fills depends upon the total number of drops falling into it in a given time.

We must introduce a further complication which it was unnecessary to mention in the case of the end organ, in the shape of a leak in the cistern. This represents the fraction of excitation which wastes away uselessly. It has quite important consequences because if the filling is slow, the height of water in the cistern will remain at a certain low level at which the leakage is exactly equivalent to the input. If the inflow is only a little greater, then the cistern will fill up further, but the increased pressure of water will make the leak run faster, and again a stage will be reached at which it becomes as great as the inflow and the level will remain steady, though higher than it was before. Only if the combined drips of the numerous inflows exceed the greatest possible leakage will the water rise to the top of the cistern and activate the automatic discharging mechanism.

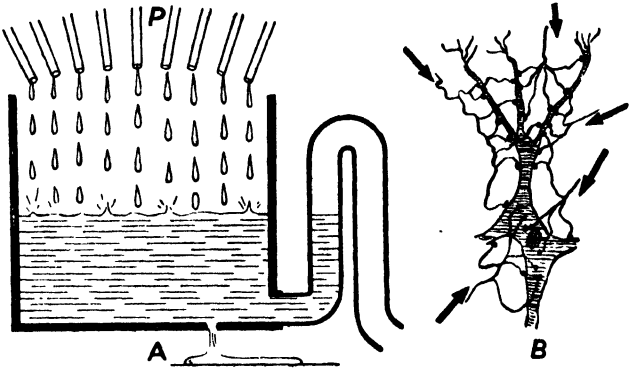

FIG. 28. A. Mode of excitation at a synapse.

The pipes (P) represent the neurones bringing excitation; and the cistern, the neurone re-transmitting excitation. For explanation see text.

B. Appearance of actual synaptic junction.

The small fibres are branches of neurones bringing excitation, and the shaded cell and fibres represent the neurone re-transmitting it.

In much the same way a neurone in a chain of neurones, even though not discharging impulses, may be in many different degrees of excitation. The most interesting stage is when the level of excitation is almost, but not quite, at the value required to create an outgoing impulse, so that for instance, an additional incoming impulse per second will be sufficient to raise it to its discharging or " threshold " value. At low levels of excitation one additional impulse per second makes very little difference.

From the analogy as far as we have taken it, it looks as though there is a tremendous convergence of impulses on the second neurone. This, however, is offset by the fact that, before terminating, the first neurone has divided up into numerous branches and connects with very many other second order neurones besides the one we have been discussing. The analogy of water fails us here because if a pipe carrying water branches, then for a given rate of flow only the same total number of drops would issue from the combined ends of the branches as from the end of the pipe if the branches did not exist. We must mix our metaphors and think again of a train of gunpowder branching: when the combustion reaches the points of divergence it ignites all the branching trains to the fullest degree. In the same way the impulse in an axon sets up fully-fledged impulses in each of its branches as the points of division are reached. There is, therefore, a mixture of divergence and convergence of impulses as excitation passes through the central nervous system.

We can see that in addition to its extensive facilities for distributing, collecting and arranging excitation into patterns, the central nervous system can step up or step down excitation. Thus, returning to our analogy of the water cistern, if the reservoir of fig. 28 is small it will emit more jets of fluid per second than if it is large. In physiological terms, the " threshold of excitation " is different in different neurones.

There are in all probability other factors modifying the transfer of excitation, but the central nervous system has one peculiarity of enormous importance which multiplies its powers of co-ordination and control. *It can actually cancel excitation.*

Inhibition

Nerve fibres carry only impulses, and we have assumed that when these reach another neurone, they transfer to it a quantum of excitation. This is not always so. Although they are no different from their fellows, impulses in some fibres, on account of some detail in the time or place of their arrival, actually *reduce* the store of excitation in the neurone on which they impinge. It is as if they were machine-gun bullets fired at the walls of the cistern, increasing the leakage of water from it, instead of being drops of water filling it. We do not know what determines that one set of impulses shall have one effect

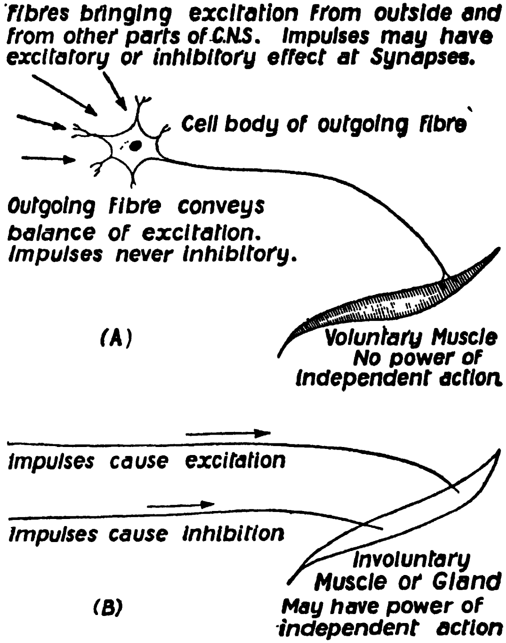
Fibres bringing excitation from outside and from other parts of C.N.S. Impulses may have excitatory or inhibitory effect at Synapses.
Cell body of outgoing fibre
Outgoing fibre conveys balance of excitation. Impulses never inhibitory.
(A)
Voluntary Muscle No power of independent action
Impulses cause excitation
Impulses cause inhibition
Involuntary Muscle or Gland
(B)
May have power of independent action

FIG. 29.

To illustrate the difference between central inhibition (A) and peripheral inhibition (B) in the control of effector organs.

and an apparently similar set the other. But it is quite certain that impulses falling upon a neurone will sometimes increase and sometimes decrease its rate of discharge. In the latter event the neurone is said to be ***inhibited***, and ***inhibition is the opposite of excitation.***

The inhibition we have described is called " central " inhibition because it occurs in the central nervous system (fig. 29A). In the control of voluntary or striated muscle (which implies the control of equilibrium, posture, movement, speech, etc.) it is the only kind of inhibition that matters. The impulses passing out of the central nervous system to striated muscle are ***invariably excitatory*** to it. If they cease, the muscle lengthens. If they increase in frequency it shortens. No impulses pass to it which *destroy* excitability. Such impulses are unnecessary, because in the absence of excitatory impulses voluntary muscle is inert, and the contest between excitation and inhibition has already taken place in the central nervous system. The nerve path to voluntary muscle is for this reason often called the " final common path " (fig. 32).

Smooth or involuntary muscle and glands are innervated differently. Two sets of nerves may run to them from the central nervous system. The frequency of impulses in each is determined in the way we have described, but when these impulses impinge upon the effector organ, one set may excite it while the other inhibits it. The final degree of activity of the organ depends on the balance between the frequencies of the two sets. Inhibition occurring like this ***in an organ*** is " peripheral inhibition " (fig. 29B).

Structures subject to this kind of control are usually capable of independent activity. Mere cessation of excitatory nerve impulses would be insufficient to put them out of action. They must be *actively* inhibited if their inhibition is called for.

CHAPTER V

CENTRES OF CONTROL

2. THE ORGANISATION OF THE NERVOUS SYSTEM

IN the last chapter we described how excitation went into the central nervous system, how it there re-excited fresh neurones and how the excitation was finally transmitted to effector organs after having been sorted out. We now need to know something a little more definite about the organisation of this co-ordinating process. Fig. 30 shows in diagrammatic form the different parts of the nervous system, each of which represents a level of control. It might be possible to sub-divide these levels and make many more or to lump some of them together and make fewer. The divisions must not be taken as indicating a big jump from one level to the next, but rather as convenient intervals at which to divide up the whole system in which each part tends to control those beneath it.

We shall achieve a fuller understanding of the functions of the individual parts of the nervous system as we study the other systems of the body, but it is possible at this stage to give in outline an idea of their relative importance.

The spinal cord

The spinal cord receives from all parts of the trunk and limbs (skin and interior) impulses which are conveyed by nerve fibres. The latter, after running with the various nerve branches and trunks (p. 53), finally distribute themselves regularly along the cord into bundles, which pass through perforations in the vertebral column and enter the posterior aspect of the cord as the *posterior nerve roots* (figs. 31B and 32). Impulses are passed out of the cord by corresponding bundles of nerve fibres arising from its anterior aspect, and called the *anterior nerve roots* (figs. 31A and 32).

These two roots join into a common trunk (C, fig. 31) a short

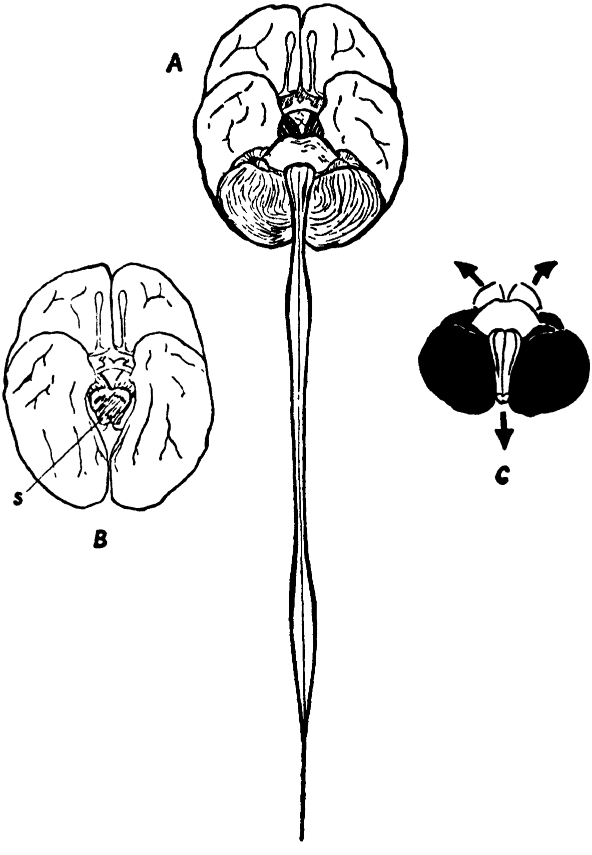

FIG. 30. A. The central nervous system as seen from in front. The brain is tilted backwards to show its undersurface.
B. The brain with the rest of the nervous system cut away at S, which is the beginning of the brain stem.
C. The brain stem (white) and cerebellum (black).

That part of A which is not shown in B and C is the spinal cord.
The two peduncles which join the brain stem to the two halves of the brain are shown in both B and C. Except for that part of the inferior surface of the brain which is covered in A by the brain stem and the cerebellum, the structures depicted in B and C can be seen in A.

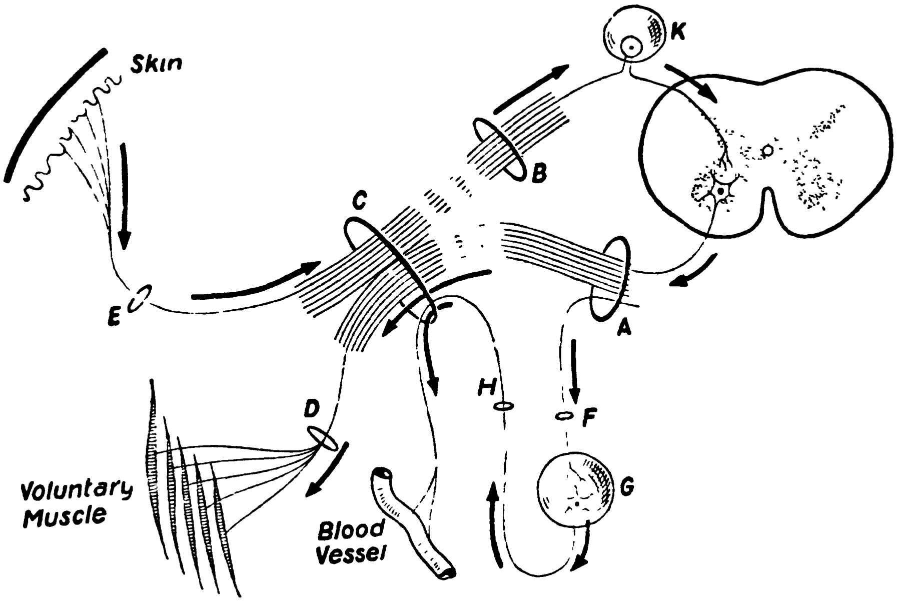

FIG. 31. Diagram showing the connections of the spinal cord. See text for details.

distance from the spinal cord. The outgoing fibres mingle with the incoming ones, and most nerves in the body carry this two-way traffic. As the periphery is approached, a certain amount of segregation occurs—for instance, nerves running to the skin (*E*, fig. 31) contain a high proportion of afferent fibres (conveying impulses towards the central nervous system). But they also carry efferent fibres (conveying impulses away from the central nervous system) to blood vessels and sweat glands. Similarly, nerves to muscles (*D*, fig. 31) contain both efferent fibres (causing the muscle to contract), and afferent fibres (recording the state of the muscle).

The cell bodies to which the afferent fibres belong are located in a little swelling, the *spinal root ganglion* (*K*, fig. 31) which appears on each posterior root just before its entry into the cord. The cell bodies of the efferent nerve fibres lie inside the cord itself. Not all the efferent fibres go straight to end organs. Some of them (*F*, fig. 31) run only as far as collections of cell bodies which lie outside the actual central nervous system as we have described it. These collections (*G*, fig. 31) are known as *sympathetic ganglia* (the adjective is of historical significance only) and they contain synapses. In them arise secondary neurones (*H*, fig. 31) which finally transmit the excitation which has arrived from the spinal cord to its ultimate destination. Many organs, though supplied by sympathetic fibres from the main part of the spinal cord, receive a second supply constructed on the same plan, i.e., a fibre leaves the central nervous system and makes a synapse with another neurone lying entirely outside the central nervous system, which finally excites or inhibits the effector organ. This *parasympathetic* supply originates either in the brain stem or in the lower tip of the spinal cord, never in the intermediate stretch which supplies the sympathetic. The cell stations of the parasympathetic, which correspond to the ganglia of the sympathetic, are sometimes also collected into ganglia, but are often scattered on or near the organ to be supplied. All organs of the body except voluntary muscle receive their nerve supply through sympathetic ganglia or parasympathetic cell stations or both. The direct one-neurone supply is confined to those very rapidly

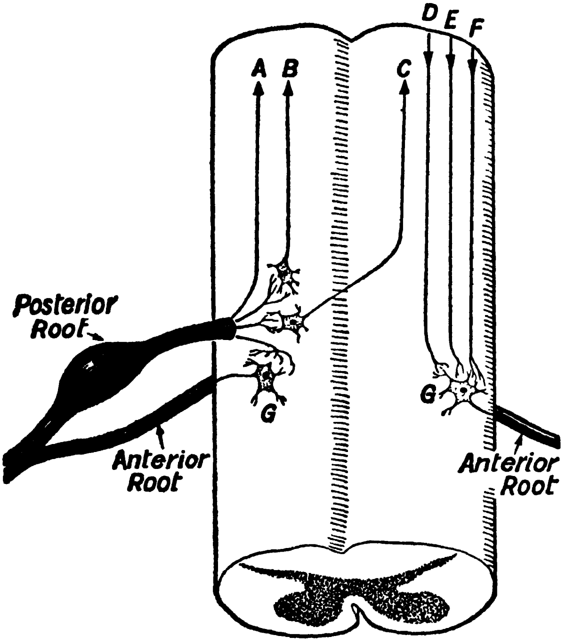

FIG. 32. This diagram indicates the way in which the spinal cord is connected to the higher parts of the nervous system.

A, B and C carry impulses upwards, while D, E and F carry impulses downwards to influence the anterior horn cell G. It will be seen that this is also influenced by local afferent fibres entering either side of the cord.

acting muscles which are under voluntary control and which move the limbs, trunk, organs of speech, etc.

The spinal cord is conveniently situated for receiving what we might term "local" information which it can deal with by itself, and which need not wait to be considered by the higher parts of the nervous system. This kind of function can be seen in a man or animal whose spinal cord has been severed, let us say, about the middle of its length. A prick administered to the foot of such a man or animal will result in rapid withdrawal of the leg from the irritant without the brain having received any information whatever. Much more complicated reactions than this are carried out locally in the spinal cord, very often by means of inter-communication between various levels within the cord itself, and concerning all kinds of activity other than movement.

In the normal intact animal and man these local adjustments or *reflexes* are subject to modification from the higher parts of the nervous system, which send fibres down to transmit impulses to the centre immediately concerned (figs. 18 and 32). If we return to our analogy of the water cistern (fig. 28) we may regard these fibres as additional feed pipes or machine-guns (p. 63) which are capable of adding or subtracting excitation, independently of the locally activated taps and leaks. The latter are thereby rendered more, or less, effective.

In addition to those fibres which are coming down from higher levels, the spinal cord also carries fibres which are ascending from the posterior roots or their neighbourhood up to the brain (fig. 32). They carry information which is of more than local interest, and, as we have already said, some of it may be translated into actual conscious sensation. This provides a parallel to the fact that some of the descending fibres can be thrown into activity by a conscious act of will.

To sum up, we may conclude that the function of the spinal cord is to carry out local adjustments by means of the cells and synapses which it contains, and to provide long nerve paths whereby the higher parts of the nervous system may (*a*) receive and (*b*) act upon the information which is pouring in from all parts of the body. The group of nerve cells with its synapses which gives rise to efferent fibres supplying a muscle is called the "*motor centre*" for that muscle. The individual neurones are called "*motoneurones*". A group of blood vessels may be controlled in an analogous way by a "*spinal vasomotor centre*", comprising a set of neurones with cell bodies in the cord which end in sympathetic ganglia (*G*, fig. 31), and which ultimately influence the diameter of blood vessels through the second neurone (*H*, fig. 31) arising in the ganglion. Sweat glands are innervated in the same way as the blood vessel in fig. 31.

Reflexes

If the same afferent path were activated on several occasions by similar stimuli, we should expect the local spinal centre to be affected on each occasion in the same way, and therefore to initiate always the same response. On the other hand, in view of the intercommunications between different parts of the spinal cord and between spinal cord and higher centres, we must allow for other sources of excitation and inhibition modifying this fundamental response so as to dovetail it into the prevailing total pattern of activity. We refer for convenience to the fundamental response as a *reflex action* or *reflex*, and we are able to identify individual reflexes because, broadly speaking, the same stimulus always elicits the same response. We must beware, however, of thinking of a reflex as a rigid inflexible unit of nervous activity. If we could take an inventory of the number and frequency of impulses and the degree of involvement of available nerve fibres, we should find that no reflex is the same on two successive occasions. *The flexibility of a reflex is its most important feature.*

The same mental reservations must always accompany our use of the classical and indispensible diagramatic representation of the " reflex arc ", comprising afferent path, centre, and efferent path (fig. 42).

The medulla, pons and mid-brain

These parts of the nervous system, frequently referred to collectively as the brain stem, contain the continuations of the fibre bundles passing to and from the higher parts of the brain, and also several important groups of cells. The co-ordinating functions of many of the latter relate to the unconscious activities of the body. Thus the movements and in part the chemical activity of the digestive tract, the diameter of nearly all the blood vessels, the rate of the heart, the movements of breathing, the balance and equilibrium of the body in space, the movements of the eyes and the diameter of the pupil are all controlled very largely from this level. Among the special sources of information discharging directly into the brain stem are the eyes (not the fibres subserving conscious vision), ears, a special organ for detecting disturbances of balance called the labyrinth, the nerves which convey sensation from the skin and muscles of the head, face and throat, and also those subserving the sensation of taste (see fig. 33).

The brain stem centres are most important for the maintenance of life, and the most easily understood example is the respiratory centre. We shall see later that the act of breathing depends very largely upon the rhythmic movements of a sheet of muscle called the diaphragm. The motor centre for this muscle is in the neck part of the spinal cord, and at regular intervals (about sixteen times a minute) the motoneurones of this centre each send out a burst of impulses. While it is receiving the impulses the muscle contracts, and we breathe in. During the interval before the arrival of the next batch the muscle relaxes and we breathe out. The interesting feature about this mechanism is that if the spinal cord is cut or injured above the motor centre for the diaphragm, these rhythmic discharges cease. Although the motoneurones themselves, the nerves in which their axons travel, and the diaphragm itself are all intact, they are incapable by themselves of maintaining respiration. The bursts of impulses which they normally emit are depending on other bursts of impulses which they themselves receive from higher up in the nervous system, i.e., from the respiratory centre proper in the medulla. In the nerve cells of this controlling centre we do find what we did not find in the motor centre, namely, " spontaneous " rhythmic activity. We put " spontaneous " in inverted commas because the cells may owe their rhythm to some rhythmic change in the environment which would take us further back in our reasoning than we wish to go. The point we make at the moment is that the rhythmic discharge persists when the respiratory centre is cut off from all the brain and brain stem which lie above it. A cat or dog whose brain has been totally destroyed above this level by a surgical operation will continue to breathe without any artificial assistance. Strictly speaking, it has ceased to be a cat or dog and is merely a " preparation ".

That there are even higher centres which *can* influence respiration is easily demonstrated by the fact that we can hold

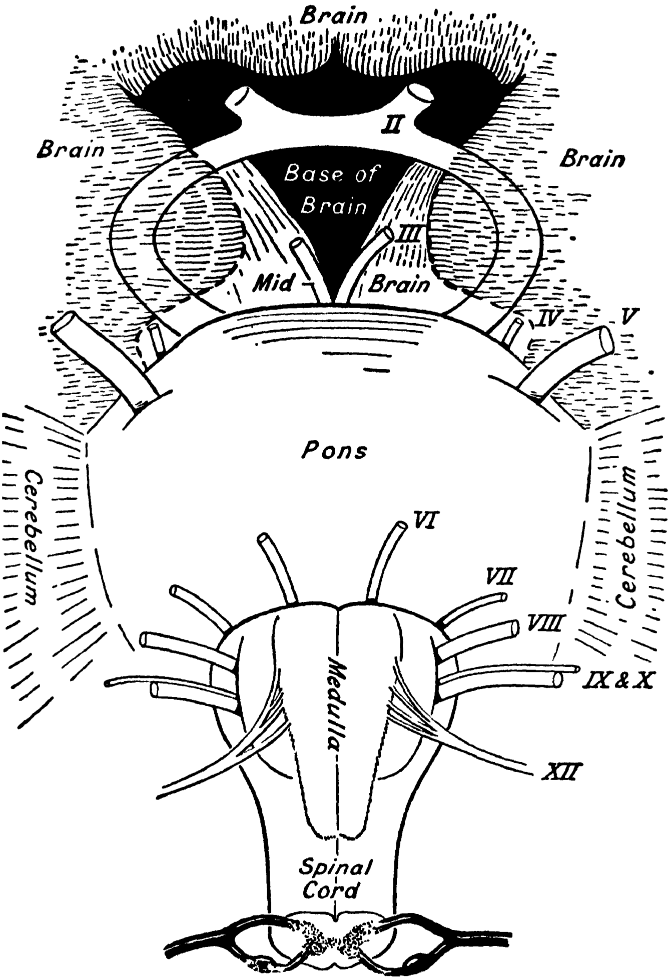

FIG. 33. The base of the brain and brain stem from beneath and in front.

Sensory nerves. II optic; V trigeminal (sensation from face and taste); VIII cochlear (hearing) and vestibular (equilibrium) divisions of auditory; IX glossopharyngeal (taste); X vagus (thoracic and abdominal viscera).

Motor nerves. III, IV, VI, to muscles of eye; V to muscles of mastication; VII, to muscles of facial expression; X to larynx, pharynx and thoracic and abdominal viscera; XII to tongue.

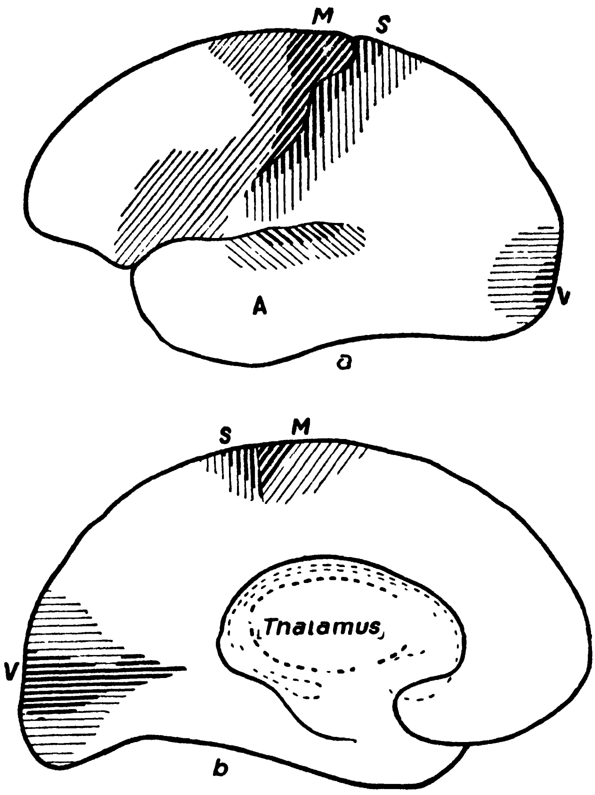

Fig. 34. (*a*) The position of areas on the outer surface of the left cerebral hemisphere known to be connected with movement and sensation.

Stimulation of the heavily shaded areas leads directly to movement or sensation; the lightly shaded areas indicate places in which arrangement or interpretation of movements or sensations occurs, the results of stimulation being less predictable.

(*b*) Similar to (*a*), but showing the internal surface of the left cerebral hemisphere; it faces the corresponding surface of the right hemisphere.

our breath or breathe very rapidly, i.e. we can, for a time, suppress or impose a new rhythm upon the motor centre. The respiratory centre can not, however, be overborne for very long: it is the real controller of respiration.

The other centres in the medulla similarly impose their control over lower centres and are themselves subject in a greater or less degree to the activity of higher centres, but we need not now discuss them individually.

The Basal Ganglia

The basal ganglia are a number of collections of nerve cells, very much larger than any of the ganglia we have mentioned so far, which represent the next level in the nervous system. They lie (figs. 34*b* and 35) beneath the cerebral cortex which represents the highest level and is a complete sheet of grey matter which covers the brain. With the basal ganglia should be included certain smaller masses of nerve cells which are embedded in the mid-brain (the highest part of the brain stem).

Most of this group of ganglia are concerned with the organisation of movement. They are much more important in lower animals than in chimpanzees and man, whose movements are subject to a great deal of direct control from the very highest level. The basal ganglia are difficult to study, but animals like dogs and cats, and to a less extent, monkeys, can perform nearly all necessary movements in the absence of that part of the cortex which controls movement in man. The basal ganglia are sometimes attacked by disease, with the result that jerky movements like those of St. Vitus dance take place, or perhaps the hands

M = Motor area.
S = Area subserving general sensation, including muscle position.
A = ,, ,, hearing.
V = ,, ,, vision.

The crumpling of the cortex into convolutions and clefts is not shown. Beneath the cortex are the masses of fibres which connect the different parts of the brain, and the brain with the lower parts of the nervous system. Embedded in this white matter, and also having numerous connections, are the basal ganglia, two of which, the thalamus and the caudate nucleus, are indicated by dotted lines in (*b*).

are unnaturally tremulous and perform rhythmic movements which are beyond the control of the will, or perhaps the posture of the body is disturbed and the normal expressiveness of the face due to the play of small muscles is replaced by a masklike stillness. From such observations of animals and men we infer that the basal ganglia play an important part in determining *patterns* of movement, and also that much of what we experience as voluntary movement can be arranged at this lower level in animals so as to meet nearly all their needs.

At least one large member of this group on each side—the *thalamus*—is, with the aid of a few satellites, a collecting ground for all kinds of *sensory* impulses. We shall see later how very important it is. Whether all the nerve impulses arriving in it give rise there to *conscious* sensation is a matter of dispute, but in the ordinary course of events this is merely an academic problem because these impulses re-excite the nerve cells of the thalamus itself and their fibres transfer at least some

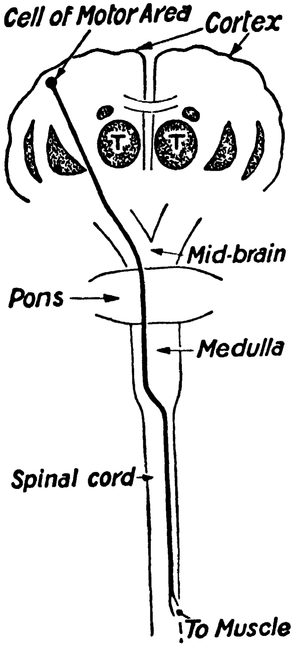

FIG. 35. Shows the course of the axon of a cell of the motor cortex, as it might appear if the cerebral hemispheres were cut by a knife passing downwards through the two ears and looked at from the front. The fibre passes between the basal ganglia (shaded) and passes into the brain stem and thence into the spinal cord to end near a cell which innervates a batch of muscle fibres. Note that it crosses the mid-line in the medulla.

of the excitation to the highest level—the cortex—where sensation is definitely translated into consciousness.

The Cerebral Cortex

As we have said, this is a thick grey mantle, composed of several layers of nerve cells and the fibres which spring from them, covering the whole brain. Its apparent area is approximately that of the inside of the skull above a line drawn round it through the eyes and ears. Its real area is much greater because it is crumpled up into innumerable folds which are generally referred to as convolutions. A deep vertical cleft divides it into the two symmetrical *cerebral hemispheres*. The connections of nerve cells in the cortex are very numerous and have not been fully worked out, but the fibres may be classified as (*a*) short and long association fibres which connect different parts of the same hemisphere, (*b*) comissural fibres which connect one hemisphere with the other, and (*c*) projection fibres which connect the cerebral hemispheres with the lower parts of the nervous system. Projection fibres may be short or long, and from what we have said it will be appreciated that in some of them impulses are passing upwards to the cortex, and in others passing away from it. Those which pass into it come principally from the thalamus and nerve cells in the other basal ganglia or brain stem, and they represent all kinds of sensation. The areas of the cortex with which the various kinds of sensation are associated are indicated in fig. 34. The fibres which pass out of the cortex convey excitation chiefly to the brain stem, and a few very long and very important ones directly to cells in the spinal cord whose fibres in turn cause the movement of muscles. It is important to realise that while the muscle-stimulating cells receive excitation from various collections of nerve cells in the brain stem, basal ganglia, cortex and cerebellum, all of them closely inter-connected, one part of the cortex (the motor area, fig. 34) can short-circuit much of this mechanism and throw muscles into activity (fig. 35). It represents the power of voluntary movement which is carried out against the backgrounds of posture and automatic movement in which the will is not directly concerned.

The Cerebellum

This part of the brain rests on the back of the brain stem and, though very much smaller, resembles the cerebrum in being invested with a layer of grey matter (nerve cells) and having other masses of grey matter embedded in its interior. Unlike the basal ganglia, however, these masses or "*cerebellar nuclei*" are almost entirely devoted to cells which receive excitation from the cerebellar cortex, and carry impulses outwards to other parts of the nervous system (fig. 36). The fibres received by the cerebellar cortex in more primitive animals come almost entirely from the labyrinth (special organ in the ear recording the body's position in space) and from receptor organs in muscles which tell of their degree of tension. This information

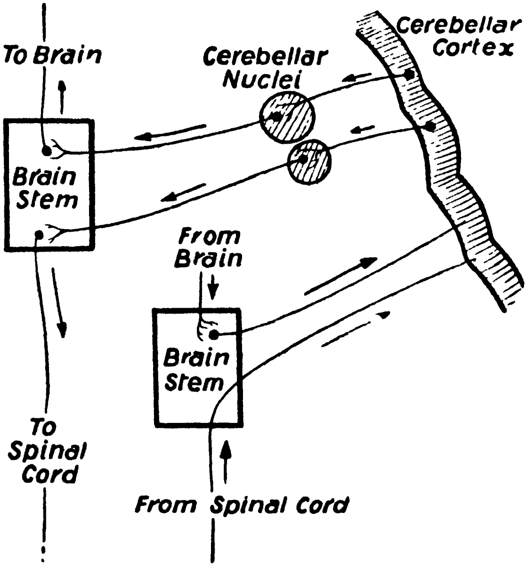

FIG. 36 shows the connections of the cerebellum with the higher and lower parts of the nervous system respectively.

is "relayed" by the nuclei to other nerve cells in the brain stem which, in turn, transmit the cerebellar influence to the motoneurones of the spinal cord, whose activity finally causes muscular movement. This system is obviously similar to that we have previously described, except that the co-ordinating organ is the cerebellum instead of the cerebrum and the information with which it deals is of a more restricted and specialised kind. Furthermore this information does not rise into consciousness as do the corresponding messages from the various sense organs of the body which communicate with the cerebrum.

In higher animals and man this particular aspect of cerebellar function is secondary. There is a great deal more cerebellar cortex, with a correspondingly large nucleus which, as before, sends impulses to cells in the brain stem. Comparatively few of these, however, send fibres down the spinal cord. Instead, their axons run upwards to the thalamus, and from there other cells carry the cerebellar influence to the motor cortex. Similarly, the information *received* by this part of the cerebellar cortex originates in cells of the cerebral cortex, whose fibres descend into the brain stem (pons). Here, they stimulate neurones whose axons go straight to the cerebellar cortex. In addition, therefore, to what might be termed the primitive function of the cerebellum in helping to maintain equilibrium, it has a much more important function in assisting in the co-ordination of voluntary movement. We do not know enough about how it carries out this function, but we do know that when it is damaged or diseased not only is equilibrium disturbed, but the muscles of the body do not act smoothly together so as to produce precisely executed movements. The disturbance is most obvious in movements involving skilled use of the hands, and in the production of speech—a very skilled movement indeed, involving the muscles of the tongue, lips, throat, etc.

The Hypothalamus

We spoke of reflex centres of the medulla which control the movements of the digestive tract, the diameter of blood vessels, the rate of the heart, the secretion of sweat, movements of breathing, etc. It now seems certain that these automatic and unconscious functions are co-ordinated by a few nuclei of grey matter lying in the vicinity of the thalamus and known collectively as the hypothalamus. Persons with disease of this part of the brain may suffer from paroxysms of sweating, flushing, palpitation, etc., which are entirely unrelated to the needs of the moment. There is also evidence that a still higher control of such functions is vested in the cerebral cortex, though voluntary control over them is absent or extremely limited. It must be constantly borne in mind that although consciousness is associated with the cortex, it is not necessarily associated with *every* aspect of cortical activity. There is an obvious possibility, however, that the function of the "conscious" parts is intimately related to that of the "unconscious" parts. It is well known, for instance, that digestion is impaired by worry and anxiety. Connections of the cortex with the hypothalamic centre presiding over the functions of the gut, and perhaps more directly with neurones supplying it, may explain this association.

It will be observed that although the control of respiration, blood vessels, heart, organs of digestion and so forth, and their smooth working together, are absolutely necessary for life, a relatively small part of the nervous system, so far as bulk is concerned, is solely concerned with such functions. On the other hand much of it is devoted to the collection and analysis of sensations from the outside world and from the muscles, and to the control, both conscious and unconscious, of the muscles so that they can work together in innumerable patterns of activity, each of which results in correct posture and smooth and steady movement. Special sets of movements like those involved in speaking and writing are extremely complex and delicate. After the areas of cortex which we know to be associated with certain types of sensation and co-ordination of movement have been mapped out, we are still left with large areas whose function is insufficiently accounted for (fig. 34).

For want of a better term they are generally referred to as the *association areas*, and they may represent somewhat higher levels of activity than those to which we have so far referred.

For instance a chimpanzee who has learnt a complicated series of manœuvres necessary to open a series of doors in order to obtain food will, if the motor cortex corresponding to one limb be damaged, clumsily achieve his object by using his sound limbs. A similar chimpanzee whose cortex is damaged in the area *in front* of the motor cortex still has an intact mechanism for the actual execution of all the movements which are necessary, but he is found to have forgotten how to set about his task, and he fails to carry it out. This kind of activity involves the execution of a pattern or sequence of patterns of movement which have been learned during his own lifetime and which are in no sense automatic. It seems, therefore, that what we commonly understand as learning requires a certain type of cortical activity, and we can nullify it by damaging a part of the cortex. This is not always necessarily the part we have cited in connection with this particular experiment.

Thinking, learning and memorising, and the communication and recording of thoughts and memories, involve cortical activity, though the nature of the relation between mind and brain is unknown. But the keystone of civilisation, namely the transmission of experience from one generation to the next, is undoubtedly dependent on the high organisation of cortical activity. This is associated with the great development of the cortex as a receiving and transmitting mechanism. It is, for instance, tremendously more developed in this respect than is the spinal cord. We have a very good idea of the relatively simple transformations, and their meaning, which are undergone by excitation passing into and out of the spinal cord, and since co-ordination in the spinal cord results in activity which can be analysed and measured, we can estimate the kind of work the spinal cord is doing even though we cannot follow out the individual nerve impulses and their fate in detail. In the cortex, however, the activity which results from the mass of information being received cannot readily be related to that information. We know that our own motives for any particular bit of activity are so complex that we should laugh at anyone who tried to account for them completely on the basis of information which had gone into the cortex during the preceding few seconds or even minutes. The whole of our previous experience is involved. Comparison, therefore, of what at any moment is going into the cortex and coming out of it fails to enlighten us on what is going on inside it in terms of nerve impulses, transformation of frequencies and so forth, and less than anything do we understand how these are associated with consciousness and conscious thought. We shall see, however, in Chapter XXI that a start has been made on this problem.

CHAPTER VI

MOVEMENT

THERE are three kinds of muscle in the body: voluntary or striped muscle, involuntary or unstriped muscle and cardiac muscle. In this chapter we are concerned only with the first. We have already referred to it in several connections.

Voluntary muscle is arranged in the form of fibres (fig. 17) which are from 1/100 to 1/10 mm. in diameter and from 4 to 13 cm. in length. They can be seen only under a microscope and, when light is shone through them, they have the appearance of being striped crosswise in alternating light and dark bands. This simply means that some of the light comes straight through the muscle to the eyes while some of it is deflected into another direction by the molecular structure of the material (chiefly protein) of which the muscle is composed. The regular repetition of a pattern of light and dark bands indicates that the underlying structure is of an orderly kind and we assume that it is related in some way to the outstanding physiological characteristics of voluntary muscle, namely, its ability to shorten lengthwise and to do this with great rapidity. *Unless provoked by some agency external to itself, it is quiescent.* In this it differs from unstriped muscle and cardiac muscle, which shorten and lengthen rhythmically even when separated from all other parts of the body and when protected from outside interference.

The agency which causes muscle to contract in the body is the nerve fibre which runs to it from the spinal cord, so that the physiological unit we should study is the nerve cell of the spinal cord *plus* its fibre *plus* the muscle fibres which, by branching, it supplies. Each nerve cell in the spinal cord innervates 100–200 muscle fibres and the whole is known as a *motor unit* (see figs. 37 and 31). Although a set of muscle fibres whose connection with the corresponding nerve cell is severed is quite inert, ***no muscle is ever completely at rest in the intact body.***

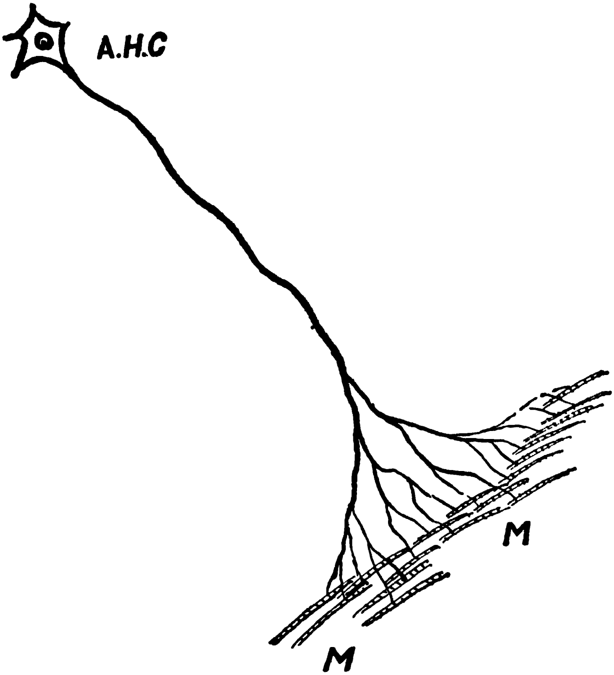

FIG. 37. The motor unit.

AHC, cell in the anterior horn of the grey matter of the spinal cord. M, muscle fibres supplied by the axon of the anterior horn cell—actually much more numerous.

The reason is that nerve impulses are always passing out from the nervous system, and each impulse adds its quota of excitation to the muscle in much the same way as the afferent fibres in the nervous system add their quota of excitation to the synaptic junction with the next neurone in the train. So far as the activation of the muscle is concerned, therefore, there is no new idea with which we have to become accustomed. The main differences between the transfer of excitation from one neurone to another and the transfer of excitation from nerve fibre to muscle are (*a*) that whereas it gives rise in the neurone which is receiving the excitation to further nerve impulses, it gives rise in the muscle to contraction. This is merely another way of stating the difference between nerve and muscle. Nerve responds to excitation by conduction and its protoplasm is evidently specialised to this end. Muscle responds to excitation by a kind of convulsion of its molecules which results in actual movement of the two ends towards each other. (*b*) No impulse arriving at a neuromuscular junction causes inhibition of contraction.

It takes more time for a muscle fibre to contract and relax than for a nerve cell to manufacture and get rid of an impulse and this contrast is readily seen in fig. 38. In the experiment there recorded the nerve supplying the muscle was cut, rendering the muscle quite inert. A single electric shock to the nerve beyond the cut produced one impulse in each of its fibres. This " volley " of impulses passed down the nerve to the muscle, causing a contraction of all the muscle fibres, and this contraction has been recorded by a pointer on a moving surface by fixing the ends of the muscle to a system of levers (see fig. 39). The electrical record of the *duration of the nerve impulse* is superimposed on this *mechanical record of contraction.*

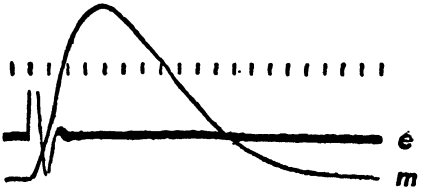

FIG. 38. Electrical (*e*) and mechanical (*m*) records of muscular contraction taken simultaneously.

Time is recorded by a vertical stroke every hundredth of a second. (Creed, Denny-Brown, Eccles, Liddell and Sherrington, *Reflex Activity of the Spinal Cord*, Oxford, 1932)

Now in the body, each nerve fibre is carrying not one but a succession of impulses to the muscle, and it is clear that, above a certain frequency, each of these will impinge upon the muscle while it is still under the influence of the preceding impulse.

The effect is to cause the muscle to contract still further. That is to say, while the molecules of muscle protein are still in the position into which they have been thrown by one nerve impulse, another nerve impulse will move them still further in the same direction, and so on until they reach a limiting position beyond which no stimulus can push them. This phenomenon is known as " the summation of contraction " and when impulses are flowing continually down a nerve fibre to muscle, the muscle goes into a degree of contraction which is proportional to the frequency of the impulses. This can best be understood by reference to fig. 40. A sustained contraction is called a *tetanus* and all contractions *in the body* are of this type. It may be objected that when the frequency of nerve impulses is very low the muscle fibres will have begun to relax before the next impulse comes along to restore the contraction. There is a danger of tremulous movements. This is so, but it must be borne in mind (*a*) that each muscle may contain two to three hundred motor units (*b*) that the individual nerve fibres

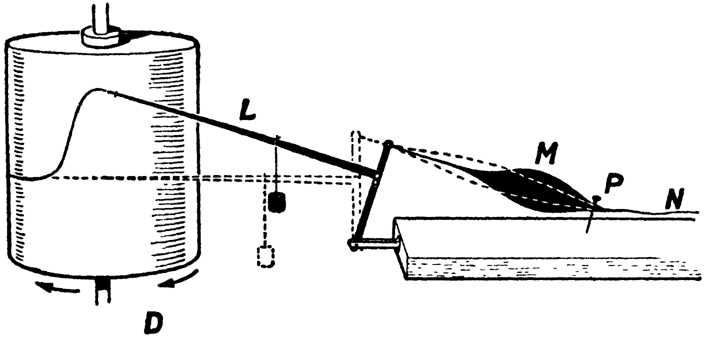

FIG. 39. A crude way of recording muscular contraction mechanically; the contraction shown in Fig. 38 was obtained with more refined apparatus.

M, muscle, removed from the body together with its motor nerve, N. P, a pin or clamp to keep one end of the muscle fixed. L, a light lever made perhaps out of a straw. D, a rapidly rotating drum. The interrupted lines show the resting, and the inked area the contracted, muscle.

are carrying trains of impulses independently of each other (compare fig. 25) and, therefore, (*c*) that at any instant no motor unit is in the same phase of contraction or relaxation as another. This results in the smoothing out of fluctuations due to the individual rhythm of the units. The muscle *as a whole* exerts a small but steady tension on its two ends.

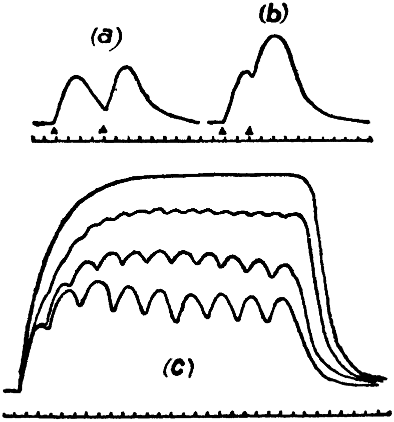

FIG. 40. Mechanical records made by muscles receiving from their motor nerves volleys of impulses in rapid succession. Time scales in hundredths of a second.

(*a*) Two successive electric shocks were delivered to the motor nerve of the muscle, each stimulating all the fibres simultaneously, at an interval of about four hundredths of a second. Note that the second muscular contraction begins before the first is finished, and that when the muscle is at its shortest it is shorter than during the first contraction. (*b*) A similar experiment in which the volleys of impulses were separated by only two hundredths of a second. (*c*) A *succession* of shocks was delivered to the nerve of a similar muscle. Four tracings are shown superimposed. The lowest frequency gives the least average degree of shortening, and the highest the maximum degree of shortening possible. Frequencies: 19 per sec., 23.5 per sec., 35 per sec., 115 per sec. (Cooper and Eccles, *J. Physiology*, 1930)

The muscles form a large part of the body and account for half of its weight. Their appearance in bulk is familiar as butchers' meat, but in the intact body they are carefully arranged in bundles or sheets and their ends are attached to bones and ligaments, in other words, to parts of the scaffolding of the body. Contraction brings their points of attachment nearer together, but it must be appreciated that the function of muscle is not always to produce *movement* even though it may be capable of doing so. Sustained contraction of a muscle may have a very important *supporting action*. For instance, the only thing which prevents our knees collapsing like loose hinges when we are standing up is the fact that certain very strong muscles pass from the front of the thigh bones to the bones beneath the knee, and keep the joints straight by a steady contraction. A *sudden* contraction of these same muscles is seen when we kick a football. Similarly the sheets of muscle which cover the abdomen, although they help to bend the trunk when we stoop down, are principally concerned in supporting, by their steady pressure, the abdominal contents (fig. 41).

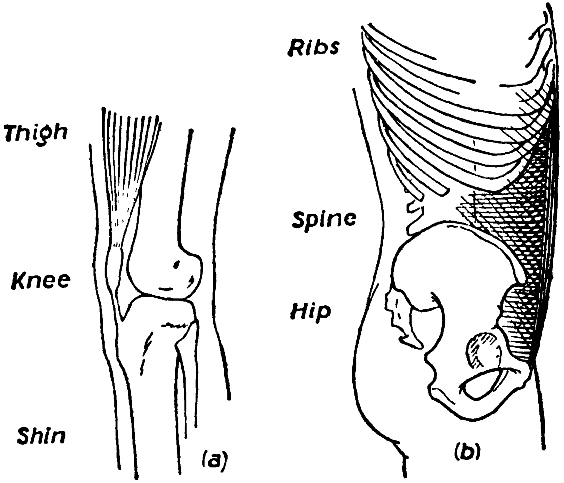

FIG. 41. To show supporting action of muscles (*a*) in front of the knee, (*b*) in the abdomen where there are several sheets of muscle with the fibres arranged approximately in the direction of the hatchings.

Although muscles are anatomical entities and have names, a given movement is very rarely brought about by the action of a single named muscle or any definite number of whole muscles. *The functional unit is the motor unit* and the reason we are able to make movements which are finely graded both in strength and direction is because a constellation of motor units in a number of muscles, some of which contribute a great many, others only a few, is thrown into action. Thus, in drawing a line with a pencil, the pressure on the point might be lessened by motor units in most of the muscles concerned becoming less active and the least active ones dropping out altogether. A change in the direction of the line may be brought about by motor units in a few muscles dropping out and others in muscles, previously relatively inactive, coming into play. The majority of units would be common to both parts of the action. *The simplest way of viewing the musculature of the body as a whole is to regard the motionless body as representing a certain pattern of activity, determined by a steady contribution from all the motor units in the body. Movement is the result of a change in this pattern.* We have gained some idea in the preceding chapter of how these patterns are arranged by the central nervous system, and it is not difficult to imagine the whole process in action.

It would be a mistake, however, to lay too much stress on the executive side of muscular contraction. As well as having motor units running out to them from the spinal cord, muscles are richly supplied with nerves carrying impulses in the opposite direction.

The function of these is to record tension, and the whole of muscular activity depends on the information which they, in common with nerves of similar function, supply to the central nervous system. The information is acted on at all the various levels of the central nervous system. Thus, the sustained contractions which we have cited as enabling us to stand are primarily spinal reflexes operating as follows: If the knees begin to bend passively under the weight of the body, then the muscles which maintain the knees straight are subjected to a stretching action. This stretch gives rise, in the very sensitive stretch receptor organs, to excitation which, in the form of an increased frequency of nerve impulses, is passed into the spinal cord. Some branches of the afferent fibres convey these impulses directly to synaptic junctions with the motor nerve cells, which, in turn, cause the muscles to shorten to their original length and maintain the knees straight. Local control is known as the *stretch reflex* (fig. 42). At the same time we know that other branches of the incoming fibres convey the information to the medulla, thalamus and cortex. In the cortex it results in conscious knowledge of the position of the knees. Yet other branches of the afferent fibres form synaptic junctions with neurones in the spinal cord which relay the information to the cerebellum where, though it does not rise to consciousness, it is essential (*a*) as the basis of any *voluntary movement* we wish to make, and (*b*) as a component of the *postural pattern* of the body upon which such a movement would be superimposed (see p. 78). In concrete terms, the result of all the information going to these higher centres is a downflow of impulses in various fibre-tracts from the grey matter of the cortex. basal ganglia and brain stem, which impinges on the

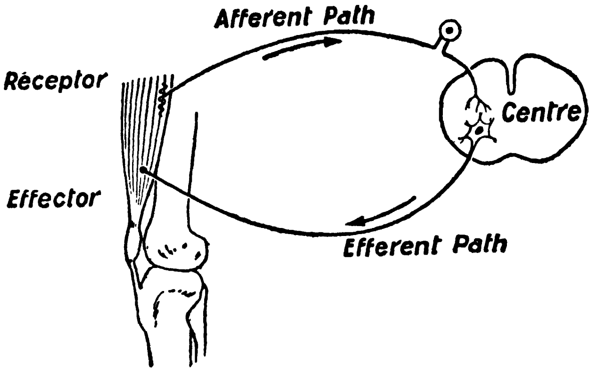

FIG. 42. The stretch reflex, illustrating the typical components of any reflex arc.

The stretch receptor is indicated by a spiral. The effector organ is the muscle itself.

local stretch reflex synapses of the cord, enhancing or damping down the local response. By damaging these tracts at various levels the degree of contraction which results from the application of local stretch to a muscle can be considerably modified. If the afferent fibres from the muscle itself are severed, then it is virtually paralysed, and of little more use than a muscle whose motor nerve has been cut—an injury which, of course, puts it completely out of action whatever other circumstances may be involved.

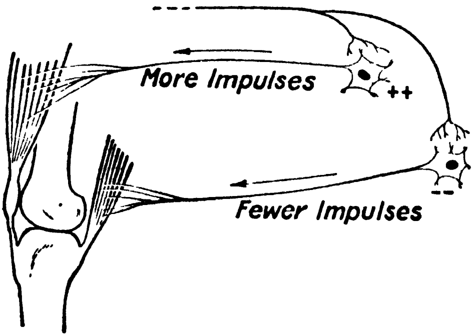

FIG. 43.

When a muscle is made to contract by reflex action, muscles which would otherwise oppose the action are caused to relax. This is brought about, as indicated in the diagram, by central inhibition (see p. 63) of the nerve cells which supply them. The number of impulses previously discharged by these cells is reduced. This type of co-ordination between muscle groups is called "reciprocal innervation".

If the muscles are cut off from all communication with the brain by an injury involving the whole width of the spinal cord above the level at which the local nerves enter and leave, they will still respond to local stimuli, and will still act in groups. That is to say, when the extensors of the knee or any other joint contract, the flexors relax (fig. 43), making a movement which is co-ordinated in itself, though co-ordinated to a very limited degree with the activity of the rest of the body. If the motor fibres (fig. 35) are interrupted as they leave the cortex, certain muscles may be paralysed in the sense that voluntary movement cannot be initiated in them, yet owing to the fact that they are still in communcation with the collections of grey matter which arrange postural patterns, they may take part involuntarily in such general movements as stretching during a yawn.

Muscle and Metabolism

Muscles, in addition to their primary function of producing movement, produce heat. We have seen in a general way that this heat is due to the combustion of fuel and that the fuel is ultimately derived from the food. We shall have to consider this subject again before we can master it completely, but, at this point, it is possible to take our enquiries a little further.

The actual fuel which is chiefly used by the muscle is a substance similar to starch and called *glycogen.* It is common knowledge that starch is a reserve foodstuff which plants store up for themselves, and for the sake of which we cultivate cereals and other vegetables. Chemically it is a large molecule which can fairly easily be broken down into a large number of smaller molecules of glucose or grape sugar. It is the basis of practically all carbohydrate foods except those delicacies which are made with cane sugar. Animals also store carbohydrate in a form which can easily be broken down into glucose, but they store it as glycogen and not as starch. The chemical difference between glycogen and starch is not important for us at the moment.

One of the places where glycogen is stored is in the muscles, and it is the food most readily available for them when they have work to perform. They themselves break it down into glucose by means of a quite complicated series of steps, involving the intervention of many other chemical substances which they contain. This series of processes is initiated in some way when the muscle is excited. The energy for the work to be done is finally provided by the oxidation of the glucose so formed, but, as we have seen, only about a quarter of the total energy produced by the oxidation is available for mechanical work. The rest appears as heat. Simultaneously with this chain of reactions culminating in the release of energy, other chemical reactions take place in the fibre whereby the shape of the long protein molecules running lengthwise along the fibre is changed.

The *immediate* chemical changes and source of energy for muscular contraction are provided by substances already present and ready for prompt action. Most of them are not actually used up in the process, but are later reconverted to their original form, so that they can undergo the same series of changes again. But as they have yielded energy in causing a contraction they cannot be reconstituted unless energy is supplied. The ultimate source of this energy is the oxidation of glucose. While the muscle is resting the glucose is, as it were, locked up in the form of glycogen and the unlocking process occurs simultaneously with the contraction process. Directly the end products of the reactions subserving contraction appear, the glucose is there ready to be oxidised and the oxidation provides the energy for them to be reconstituted.

In prolonged contraction it is easy to see that while some molecules are being broken down, others are in process of reconstitution, and so long as the supply of glucose is maintained, the muscular work can continue. It is unusual for work to be so severe and prolonged as to exhaust the actual glycogen stores of the muscle, but in any case these stores are constantly replenished from the blood stream.

It is important to appreciate this series of relays in the supply of energy for contraction, because it is clearly possible for a certain amount of muscular work to be done without a supply of glucose or oxygen. So long as the materials which are of immediate necessity for the contractile process remain available, then that process can take place. Experiments have been made in which the breakdown of glycogen to glucose has been arrested without interfering with the other chemical processes going on in the muscle. In these circumstances, the muscle contracts under stimulation for a certain length of time and then comes to a standstill. Similarly, if the chemical mechanisms are left intact but the supply of oxygen is withdrawn, contraction will again take place and finally stop. Under these conditions, provided the muscle is not driven to extremes, oxygenated blood can be admitted to the muscle, and by oxidising glucose it restores its capacity for contraction. In other words, we have obtained the work from the muscles first and repaid it, in terms of energy, subsequently. In a later chapter we shall see that this property of muscle is extensively made use of.

A digression

The processes going on in muscle give point to an important general principle. Although outside the body it is quite easy to convert glycogen into glucose by the use of heat and fairly strong chemicals, such crude methods would be impracticable in the body. Whatever the body has to do must be done at a temperature of about 37°C. and with the mildest possible chemical reactions. For this reason, many apparently simple transformations are made by what seem to be unnecessarily numerous and small steps. On the other hand, these same methods seem to bring about other transformations which are extremely difficult (and sometimes impossible in the present state of our knowledge) to make outside the body. To understand this more fully the reader cannot do better than read the fascinating book by Kermack and Eggleton entitled *The Stuff We Are Made Of*.

In the absence of heat and powerful reagents, the chief instruments which the cells of the body use are *enzymes*. These substances are complex, sensitive, easily destroyed and easily rendered inoperative. Their function is to facilitate and speed up the chemical intercommunication between substances which would otherwise lie side by side without greatly influencing each other. The enzyme remains unaffected by the chemical process it encourages, and once it has dealt with one batch of molecules is ready to perform its task again with another batch.

Enzymes are so delicately constituted that they are specialised to do one thing and one thing only. For instance, an enzyme capable of introducing water at strategic points into the large glycogen molecule so as to break it up into smaller constituents is quite unable to insert water into any other kind of molecule, for which purpose a separate and also highly specific enzyme probably exists. The majority of the small steps by which chemical reactions occur in the body are carried out in virtue of the presence of enzymes which act only when the appropriate molecules are presented to them. The result of one step provides the raw material for the next and so forth until the whole chain is complete.

Still speaking of the body as a whole, it is probably true to say that many of these chains of reactions are in progress continuously, but there are many which are dormant until thrown into activity by some special stimulus, such as that which causes muscular contraction. The way in which the first link in the chain is completed in these cases remains a mystery. Enzymes are not always concerned in *breaking down* large molecules into small ones, or in making use of the stored resources of the body. The characteristic kind of protoplasm of which any cell is made, foodstuffs in a form suitable for storage, and certain powerful drug-like chemicals, are largely *built up* from raw materials by means of specific enzymes.

The cells of the body are divided from each other by surfaces, and the tendency of certain molecules to congregate on certain types of surface is thought to be another way in which reacting molecules can be brought so close to one another that they react under conditions of temperature, etc., in which they would ordinarily remain inert.

Returning now to the utilisation of stored glycogen, it is quite clear that such a store unless replenished would otherwise become exhausted, and from the chemical point of view it is almost unnecessary to say that the store is being continuously built up from glucose during periods of relative inactivity. A question which we must put down for early consideration is the means by which glucose is supplied to the muscle in sufficient quantity.

CHAPTER VII

THE STRUCTURAL AND FUNCTIONAL ORGANISATION OF THE BODY

BEFORE we can further consider the questions which have been raised in the course of the preceding chapters we must gain some idea of the division of labour between the various parts of the body, and the fundamental relation in which they stand to one another.

The ultimate unit of living matter is a collection of protoplasm known as a cell, the life of which depends on a specialised structure, also protoplasmic and called the *nucleus*, under whose sphere of influence it comes. Protoplasm is just another name for living matter and is known rather for what it does than for what it is. When in the form of a cell it has certain characteristic properties.

(1) When mechanical, thermal, electrical or chemical stimuli are applied to it, its state of activity changes; for instance, a nerve cell produces a nerve impulse and a muscle cell contracts. Protoplasm therefore possesses the property of *irritability*.

(2) Excitation is conducted to all parts of it. *Conductivity* is best seen in nerve cells.

(3) It possesses the power of *movement*. This is best seen in muscle cells.

(4) It can perform *chemical reactions*, some of which are very specialised (e.g. the production of certain active chemical substances), but which must always include the general reactions concerned in the oxidation and utilisation of foodstuffs.

(5) It uses oxygen and evolves carbon dioxide—*respiration*.

(6) It has the power of adding to its bulk and multiplying the number of its units—*growth* and *reproduction*.

It will be seen that these properties are not isolated but that some of them overlap. Conductivity, for instance, is in a sense a special instance of excitability. Some of the chemical processes imply respiration, and growth also implies the power to deal with raw materials chemically. The terms we have defined are, however, conventionally used to express ideas which by experience have been found useful in describing the activity of living things. Classification itself is a secondary matter.

The study of nature tells us that it is very difficult to draw the line between non-living physico-chemical systems and living protoplasm. Up to quite recently it has always been taken for granted that the most primitive type of organisation is seen in unicellular organisms, such as the very minute bacteria or better still in the larger specks of nucleated protoplasm which live in ponds. We now know, however, that certain agencies ("viruses") with which we are chiefly familiar because they produce diseases of plants and animals, notably the common cold, do not partake of the protoplasm-with-nucleus type of structure Some of them have, in fact, been obtained in the form of crystals. Yet they show many of the characteristics of life, and are the nearest approximation we know to a link between the non-living and the living. They are so very small that the usual methods of microscopic study cannot be applied to them.

If we take the little unicellular organism, *Amoeba,* from a fresh-water pond we can show that this one speck of protoplasm is capable of all the types of activity we have listed. It has no specialised parts, and every part of it is irritable, will conduct excitation, and can move, respire and act as a chemical laboratory. It can also grow, and it multiplies the number of its units by splitting in half in such a way that the two offspring contain part of the protoplasm and also part of the only specialised structure, the nucleus. (Separated from the nucleus, protoplasm dies, a fact which we have already remarked upon in connection with nerve cells.) We will not describe experiments on the amoeba to prove these facts. The interested reader will have no difficulty in finding them elsewhere. One property, that of movement, does repay somewhat closer attention, not because it is more important than the others, but because it survives in certain cells of the blood. It is also useful in showing by contrast how beautifully specialised and highly developed is the kind of movement we have described as occurring in voluntary muscle.

When an amoeba moves over a surface a tongue of protoplasm is pushed out in the direction of the movement to a certain distance, when it seems to fix itself to the surface until the rest of the protoplasm which lies behind it has caught it up and flowed round it. Another tongue may be thrust out and the movement continued. The shape of the amoeba is quite irregular during progression and the first movement may be made by any part of its surface (see fig. 44).

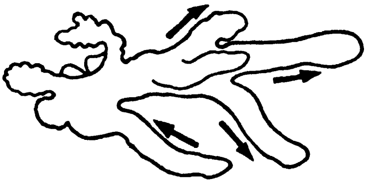

FIG. 44. Outline of an *Amoeba*, showing the tongues of flowing protoplasm (pseudopodia) by which it moves.

Every cubic millimetre of blood contains 5,000 to 10,000 "white cells" (fig. 51), which float about in it as individuals. Most of them possess the power of amoeboid movement, which enables them to prize apart the plate-like cells composing the walls of capillary blood vessels and to enter the tissue fluid (pp. 99–104). They do this in large numbers at any point in the body which is invaded by bacteria. They engulf the latter together with some of the debris occasioned by the destructive activity of the invaders. The white cells (*leucocytes*) should not be confused with the haemoglobin-containing red cells (*erythrocytes*) of the blood which exist in much larger numbers.

As we move higher up in the animal scale, organisms cease to have merely one cell but consist of aggregates, which means that a proportion of the cells are cut off from direct communication with the environment. Some are so placed that their power of movement would embarrass the parent organism, some, particularly those on the exterior, are in an admirable position for receiving stimuli, others are suitable for support, and so on. Consideration along these lines will show that small development in the way of increasing bulk could take place without some functions of certain groups of cells becoming specialised at the expense of other functions. This, in fact, is what we find. The cell, though still a unit, becomes subsidiary to the larger unit of the organism as a whole, and in consequence the unfolding of its properties in their various special directions becomes very interesting. Nevertheless, having indicated the broad lines upon which living matter has developed, we shall skip the details and consider specialisation of function in the cells of higher animals and man.

The great difficulty raised by aggregations of large numbers of cells to form *tissues* in the higher animals is the supply to them of oxygen and nutritive materials. A single-celled organism like the amoeba is completely surrounded by its nutritive fluid and, as it lives at a fairly low temperature, its nutritive processes proceed so slowly that it can pick up sufficient oxygen from the water in which it lives to maintain life and activity. In warm-blooded animals like ourselves, the aggregation of cells is further complicated by the high temperature at which they live and the greater amount of oxygen and food which they consequently require. We have seen, moreover, that many of them are very highly specialised, and although the chemical reactions underlying this specialisation are by no means all worked out or understood, it is quite certain that they are very much more delicate than those of the amoeba and easily impaired by a small change in the temperature or chemical composition of their surroundings. The mammalian cell has, therefore, three serious problems which do not concern the unicellular organism at all. (*a*) The cells are aggregated into masses. (*b*) They live at a higher temperature. (*c*) Their chemical processes are more easily upset. If the *amoeba* finds itself in an unhealthy environment it can move away to a more congenial spot. The mammalian cell cannot do so.

One of the main principles of physiology, which was most clearly enunciated by the great French physiologist, Claude Bernard, runs as follows: " La fixite du milieu intérieur est la condition de la vie libre." This means that *given* a controlled environment in which to live, the cell can devote itself freely to its specialised task without having to think continually of its own bread and butter.

In one way or another, either by minute channels running between them or otherwise, the cells of the body are bathed in a fluid which pervades all the tissues. It may not be very obvious and in places may be little more than a film, but it exists nevertheless and every cell of the body has fairly direct access to it. We can, if we wish, imagine that the *body* consists of cells only and that the *environment* in which they live is this "extra-cellular fluid." Now, in an imaginary scheme of this sort, we find it difficult to create a satisfactory working system in our minds because we are familiar with the solid aspect of tissues in microscopic section, and common sense tells us that if these are permeated by fluid the fluid will in places become stagnant. In more precise terms, cells which are working hard or living at a fast rate will tend to accumulate waste products around them, and if these are poisonous the cell will continually have to pause until the waste gradually seeps away. This would not be in accordance with the pace at which warm-blooded animals live, and, in fact, the extra-cellular fluid is always being very thoroughly stirred by the now familiar device of the circulation of the blood (fig. 45).

We can leave the mechanics of the circulation until later. There is no reason why we should not take for granted that the body contains a system of tubes, the blood vessels, in which

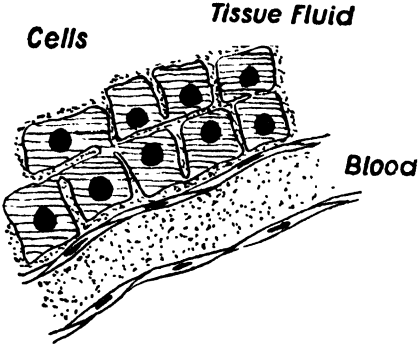

FIG. 45. Scheme of relationship between intracellular fluid (shaded) and extracellular fluid (stippled).

Part of the latter bathes the cells and is known as tissue fluid, and part circulates in the blood vessels as blood plasma. Blood plasma differs from tissue fluid only in its protein content. The walls of the capillary blood vessels offer no obstruction to the passage of water and dissolved substances, with the single exception of the plasma proteins. The blood cells, which are suspended in the plasma, do not enter into the relationship and are neglected.

blood is rapidly circulating. The most obvious part of the blood vascular system consists of the larger vessels, a gross transport mechanism in which we are not at present interested. The business end of the circulation lies in minute channels, the *capillaries* (fig. 46), which are invisible to the naked eye and

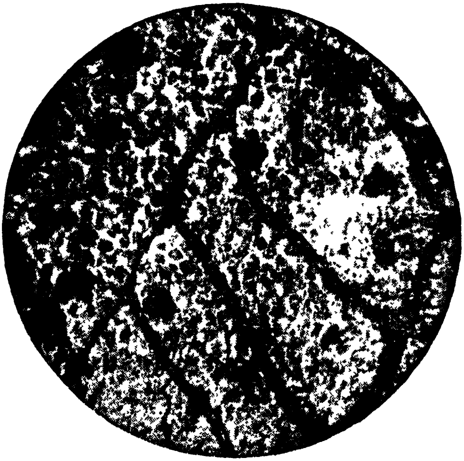

FIG. 46. Photomicrograph of a tadpole's tail showing capillaries containing corpuscles (× 100).

which, historically, were not actually seen until the fact of the circulation of the blood had been established. Nowadays we can see them quite easily, and cinematograph pictures have been taken through their transparent walls of the blood flowing in them. Their diameter is very variable, but if we think of them as being one hundredth of a millimetre wide we shall not be far from the truth. Their walls are made of pavement-like cells whose surface is quite extensive, but whose thickness is negligible. *The protoplasm of which they are made has the property of allowing water and nearly all dissolved substances to pass through it.* Only the solid elements of the blood (the blood cells, fig. 51) and some proteins in solution whose molecules are very large—perhaps comparable with the molecules in the protoplasm of the capillary walls—are held back. Except for these dissolved proteins, the fluid bathing the cells and that circulating in the blood vessels are in free communication.

There would clearly be something very intangible about the circulation of a fluid in tubes which did not hold it in. In fact, the circulation of the blood would become pointless. One has only to think of a large tank of water through which passes a tube carrying another system of flowing water, and then think what would happen if the pipe inside the tank were replaced by a piece of pipe-shaped wire mesh. There would be no mixture in the first case and a very complete mixture in the second.

The proteins dissolved in the blood—*the plasma proteins*—enable a very important compromise to be struck. They have the property of holding on to the water in which they are dissolved so that work has to be done to separate it from them. The pressure which is forcing the blood round is, in the first part of the capillary, sufficient to separate some of the fluid from the plasma proteins and to push it through the capillary walls into the tissue fluid. But by the time the blood has reached the other end of the capillary, this pressure has been reduced by friction and loss of fluid to a point where the plasma proteins are able to attract water back. In this way a constant exchange is kept up between blood and extra-cellular fluids (fig. 47). At the same time the balance between the average mechanical expulsive pressure and the attractive (osmotic) pressure of the plasma proteins is such that the quantity of fluid in the blood stream never falls below a certain minimum

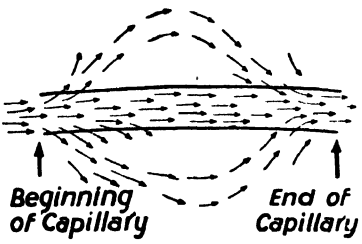

FIG. 47.

As the mechanical pressure driving blood along a capillary falls, the plasma proteins are able to attract fluid into the blood stream. This replaces fluid driven out of the blood at the beginning of the capillary while the pressure was high. The diagram shows how this causes a mixing of blood plasma and tissue fluid.

value. It is always sufficient to keep the plasma proteins in solution, to keep the formed elements of the blood comfortably in suspension, and to maintain a sufficiently low viscosity for the blood always to flow freely.

The tissue fluid is in this way kept thoroughly " stirred " by the blood, for all parts of the body are very richly supplied by capillaries in much the same way as a city is richly supplied by streets. There are no cells very far from a capillary, just as there are no houses very far from a street. About 8 per cent of the body weight is blood, so that a 70 kgm. man has about 5½ litres. The volume of tissue fluid is about 14 litres. these figures are only approximate but they give us a good picture of the degree of " stirring " to which the tissue fluid is subjected and also show that the total bulk of fluid in which the tissues live is a relatively small proportion of the whole body: 5½+14 is 19½ litres. Although the whole of the blood circulates, the blood cells or corpuscles which float about in it occupy half of its volume. Thus the actual amount of free fluid represented by blood and extra-cellular water is only about 17 litres, weighing 17 kgm. Of the remaining 53 kgm., including the blood cells, about 30 are water, but this water is in the cells themselves, which represent the " stationary " part of the body. In other words, for each part of the fluid in the body which is either circulating or well stirred by the circulation, i.e. which constitutes the environment in which the cells live, there are nearly 2 parts inside the cells. This is the *intra-cellular water*. Molecules of water itself and of *certain* dissolved substances, particularly oxygen, nutritive substances and waste products (including carbon dioxide) can pass freely through the cell membranes, and in fact the life of the cell depends on this exchange. There is a great difference, however, between most of the dissolved substances in the water inside and outside of the cells, in contrast to the similarity of composition on the two sides of the capillary wall.

The working cells of the body, therefore, live in an immediate environment which is less bulky than they are themselves. It is as though they were covered by a layer of environment. We have mentioned that it is necessary, if the life of the cells is to run smoothly, that this immediate environment should be constant in temperature and, as far as possible, in composition. It is obvious that such limited surroundings would themselves be quite inadequate as a store of raw material for the activities of the cells. If they did act as a reservoir their composition would change very rapidly. These considerations lead in a rather roundabout way to the conclusion which the reader has already drawn for himself, and in any case knows by experience, that this limited "internal" environment is itself in contact with the wider environment in which we live. The "external environment" is the real *storehouse* of raw materials, while the "internal environment" serves the double function of providing a constant medium in which the body lives, and of acting as a *transport agency* between the external environment and the cells.

We are led inevitably to the further conclusion that the internal environment must take up materials from the external environment at much the same rate as these are used by the tissues, and it must transfer the waste products of tissue activity to the exterior at the same rate as these are produced by the cells. Otherwise its composition would undergo large fluctuations. It would be an extraordinary medium which could do this by itself, and we find that a *high proportion of the cells and tissues of the body are actually engaged in regulating the contacts* (using this word in a very wide sense) *between the internal and external environments.* We have a circle of activity. In order that the working parts of the body should live they must have stable surroundings, but a great part of their life is devoted to ensuring this stability. Some organs do nothing else. Having grasped this very important fact we may now glance in turn at the various parts of the body and try to gain an idea of how they fit into the general scheme.

1. The circulation

As we have said, the vital part of the circulation consists of the capillary blood vessels, but in order that the blood may be kept flowing in these, tubes leading to them and from them are necessary and these are known respectively as arteries and

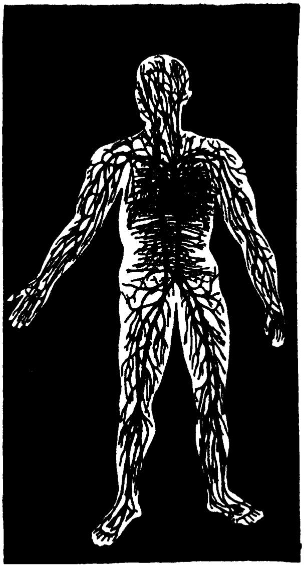

FIG. 48. General diagram of the distribution of blood vessels.

veins. The heart is composed almost entirely of muscle which is arranged in the form of a pump, so that the blood which returns to it in the veins is forced out of it into the arteries at a pressure high enough to drive it through the arteries and capillaries. The proper distribution of blood between various parts of the body is carried out by the opening and closing of small arteries which act like sluices, but the switching of blood from one part to another is rarely a quantitatively exact reflection of tissue activity. Frequently it is by itself insufficient. The active organ needs a greater supply of blood per minute than can be ensured by simply opening up its vascular supply, and the volume of blood flowing through it per minute may have to be further increased. Such variations as this in the demands of the body are met by an adjustment of the rate and output per beat of the heart. In our study of the circulation we shall study the adaptations of the heart and vascular system in more detail (Chap. VIII).

2. The respiratory system and red blood cells

The respiratory system deals with the uptake of oxygen by the blood and its delivery to the tissues. Its plan is simple. The windpipe or *trachea*, which opens into the throat and can be felt in the front of the neck, branches into *bronchi*. The bronchi branch and branch again and again, the final branches ending in minute air-sacs or *alveoli*. Each of these is covered by a network of capillary blood vessels. While the fundamental plan is correctly shown by fig. 49, the whole arrangement of tubes and sacs is so packed that the spaces in the diagram between the alveoli are actually occupied by other alveoli. The capillary blood vessels therefore have alveoli on all sides. There are two main collections of tubes, alveoli, and blood vessels, known as the left and right lungs, which together fill the whole of the chest, except for that part occupied by the heart and great blood vessels.

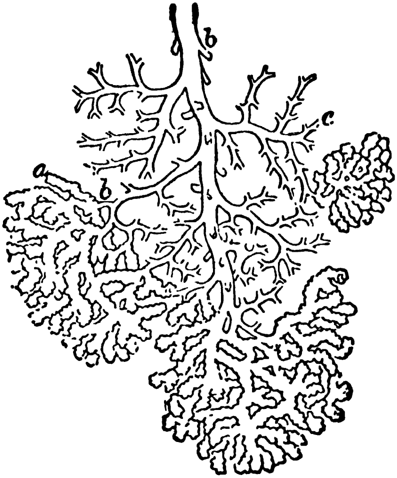

Fig. 49. Small fragment of lung. Diagram showing how an air tube branches and ends in air sacs.

(*a*) Air sacs. (*b*) Bronchial tube. (*c*) Smaller bronchial tubes.

The capillary blood supply to the lungs is very rich indeed and the capillaries are in intimate contact with the air, which furnishes our reservoir of oxygen. The actual surface of blood thus exposed to the atmosphere is said to be about the size of a tennis court. We shall have to describe this more fully later, but it is perhaps worth remarking now that the branching of air tubes leading into the depths of the lungs is so profuse that there is a certain delay in the rate at which molecules of oxygen penetrate from the outside atmosphere to the neighbourhood of the blood vessels, and at which carbon dioxide migrates from the blood to the exterior. This means that the atmosphere in the depths of the lungs contains more carbon dioxide and less oxygen than is found in atmospheric air (fig. 50). The alveolar air, as it is called, is also saturated with water vapour and is at body temperature.

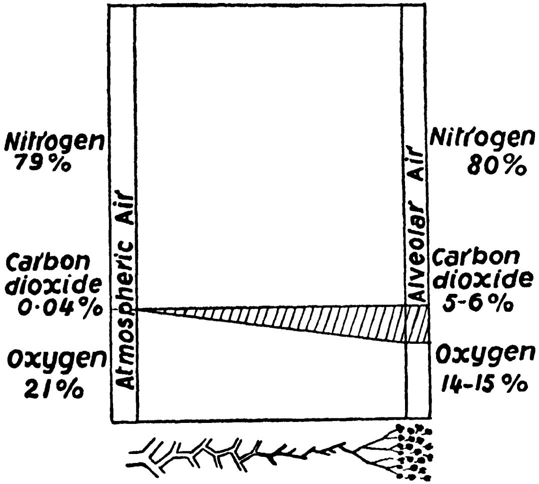

FIG. 50. Showing the relationship between the atmospheric air and the air to which the blood is exposed (alveolar air).

Owing to the structure of the lungs the latter is maintained practically constant in composition, in spite of its difference from atmosphere air. Space occupied by carbon dioxide shaded. (The space taken up by water vapour is ignored.)

A small tide of atmospheric air washes backwards and forwards against the alveolar air, and the rhythm of ebb and flow, with which we are familiar as the act of breathing, is accelerated or decelerated in such a way as to keep the composition of the alveolar air constant. Just as the tissue fluid and blood are maintained constant in composition so as not to embarass the tissues (p. 100), so we have in the lungs a kind of secondary environment, this time made of modified air, so that the exchange of gases between the blood and the exterior runs with maximum smoothness. For the same reason as we shall have to study the control of heart and blood vessels in the circulatory adjustments which serve the tissue fluid (Chap. VIII), so we shall have to study in more detail the control of the respiratory movements which regulate the alveolar air (Chap. XII).

When the blood leaves the lungs it goes to all other parts of the body, where oxygen is abstracted from it and carbon dioxide returned to it. The amount of oxygen which the tissues gets depends on the amount which the blood contains, the proportion of this which can be abstracted, and the volume of blood which is supplied per minute. The quantity of oxygen which can be brought to the tissues depends not only on complete aeration of the blood in the lungs, but on the amount of oxygen-carrying material which it contains. This material is a very important red pigment known as ***haemoglobin***. If the amount of haemoglobin in the blood is less than usual, then, other things being equal, it will be necessary for the circulation to be speeded up in order to pass on the same amount of oxygen as formerly to the tissues. This means that the heart has to work harder. But the heart itself is depending on the oxygen supplied to its muscle, and its reserve of power will be less than the normal. This is a good example of how the various systems of the body are interdependent.

The haemoglobin of the blood does not exist free in solution in the plasma, but is confined to the ***red blood corpuscles*** or ***erythrocytes*** (fig. 51). These are minute discs, about 8 thousandths of a millimetre in diameter, which float in the plasma

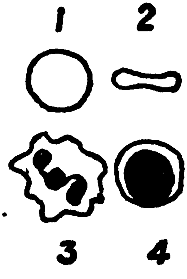

FIG. 51. Blood cells.

1 and 2: Disc-shaped red cells, seen flat and in profile. There are 5 million per cu. mm. 3. White cell, capable of amoeboid movement; about 6,000 per cu. mm. 4. Lymphoid white cell, found also in lymph (p. 196) and lymphoid tissue (p. 145), about 2,000 per cu. mm

and give blood its red colour. Each cubic millimetre of blood contains between 5 and 6 millions of them, and their combined volume when pressed together is equal to that of the plasma in which they are suspended.

3. The digestive system

In addition to the special department of the circulation arranged for the contact of blood with air, a very large department is set apart for the collection of the raw materials for replacing wear and tear of the tissues and for supplying fuel. We again have a cushioning system, this time between the blood and fuel in its natural state. It is chemical rather than physical in nature. Instead of a blind alley like the lungs, in and out of which the environment washes like a tide, we have a tube which passes right through the body from mouth to anus, so that the food can be put in at one end and the waste products excreted at the other.

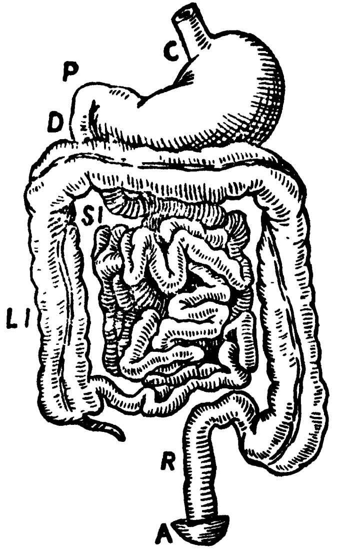

FIG. 52. Alimentary tract comprising in order

C, cardiac end of stomach. P, pylorus. D, duodenum. SI, small intestine. LI, part of the large intestine or colon. R, rectum. A, anus.

The food as we eat it is in the form of large molecules which may be suitable for storage but not for transport in the blood stream. While they are in the digestive tube, ***alimentary tract*** or ***gut*** (fig. 52), these large molecules are broken down into much smaller ones by extremely active chemical fluids, a process known as *digestion*. As digestion takes place, the capillary blood vessels lying close beneath the inner surface of the tube are able to absorb the small molecules of food, which are then carried to all parts of the body in the blood stream. In addition to the blood vessels, there is a system of capillaries containing tissue fluid, which ultimately empties itself by a duct into the blood stream, and some of the food molecules pass into the circulation through this channel (fig. 80).

The manufacture of the active digestive fluids is in itself a a major undertaking, and a great part of the activity of the alimentary canal is devoted to their production. Some of them are made in special collections of cells which pour their products by means of ducts into the main digestive tube.

In addition to its chemical and absorptive activities, the gut must also propel the food from one end to the other, and the coating of the tube is muscular in nature, its movements being co-ordinated by a rich network of nerves. We shall clearly have a great deal to think about when we come to study the process of digestion.

Before the absorbed foodstuffs in the blood stream go anywhere else they have to run the gauntlet of the great chemical laboratory of the body, namely, the liver (fig. 53). In fact, the blood which has already been collected into veins from the gut is distributed again throughout the liver in a second system of capillary blood channels before being re-collected into veins and passing to the heart for final distribution. The activities of the liver are extremely important. Fundamentally, we may regard it as a second cushion between the blood-tissue fluid system and the exterior, but it performs other functions as well.

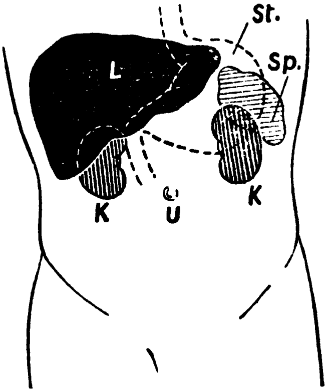

FIG. 53. The relative position in the abdomen of the liver (L), stomach (St.), spleen (Sp.) and kidneys (K). U shows the position on the skin of the navel or *umbilicus*.

4. The excretory system

The excretion of waste products has already been mentioned. Carbon dioxide is excreted through the lungs, and those parts of the food which are unsuitable for digestion are simply passed out of the lower end of the alimentary tract. The oxidative processes which go on in the cells, however, produce waste products of another kind. These are chemical substances which are passed by the cells in watery solution via the tissue fluid into the blood stream and they must not be allowed to accumulate. The blood is cleared of them by a special pair of organs called the kidneys (fig. 54) which are extremely sensitive to its composition. The kidneys act upon the blood in such a way as to abstract waste products from it and to pass them into about two million narrow channels, comparable in size to capillaries, which join together as the twigs of a tree might be regarded as joining together to form larger and larger ducts which finally lead to the exterior. Here again we have a cushioning effect, once more of a physical nature. The waste fluid does not drip to the exterior as it is formed but is collected up in a hollow organ, the urinary bladder (fig. 54), which is emptied five or six times a day.

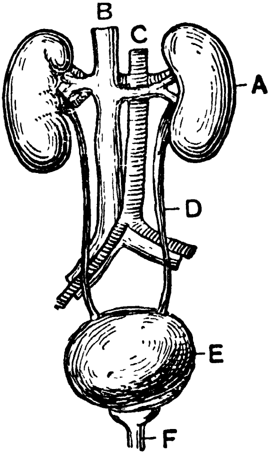

FIG. 54. Diagram to show: A, kidneys; B, inferior vena cava receiving renal veins; C, aorta giving off renal arteries to kidneys; D, ureters; E, bladder; F, urethra which opens externally.

One of the most important functions of the kidney is to get rid of the unwanted products with the minimum waste of water. We have seen in connection with temperature regulation that water is continually seeping through the skin and being evaporated, even when the sweat glands are not active, and a certain amount of water is also lost in the breath, which is saturated with water vapour. But the solid waste products which are passed out of the body by the rectum contain the minimum amount of water, and the urine which is passed out by the bladder is as concentrated as possible.

In the same way that the proteins of the blood exert an attraction on the fluid in which they are dissolved, so do all other dissolved substances. So far as the relation between capillaries and tissue fluid is concerned, only the proteins matter, because the concentration of the other substances on each side of the capillary wall is continually being equalised. In the kidneys, however, water has to be withdrawn from the solution of waste products until they are several times as concentrated as they are in the blood, and this requires a great deal of work on the part of the cells. They have to act as minute physico-chemical pumps and how they do this we do not know. We know only that they require a rich supply of oxygen in order to carry out their task.

5. The nervous system

We have already considered the nervous system in some detail and it is only necessary at this point to draw attention to the number of times in the last few paragraphs we have had to refer to, or imply, adjustment of activity to meet the needs of the body. Much of this adjustment is brought about by the nervous system.

6. The endocrine system

Scattered in different parts of the body are relatively small collections of cells whose task is to manufacture chemical substances which are passed directly into the blood stream and carried to all parts of the body. Some of the substances have a local action, some a general action; sometimes the action is short-lived, sometimes it is continuous. These collections of cells are known as the *endocrine organs* or *ductless glands*. In general, they also have the function of co-ordinating activity with requirements.

7. The voluntary muscular system

The reader will have noticed so far that we have considered each of the systems in turn in relation to their function of keeping the internal environment constant and, in fact, they seem principally devoted to this end. The question arises, does the body do anything else but keep itself going? If pursued too far this question would lead us into the realms of philosophy, but we are permitted to be a little short-sighted and say that the voluntary muscles enable us to act positively upon our environment. A great part of the nervous system is devoted to the collection and sorting out of information which is then used to determine the momentary pattern of activity of the voluntary muscular system. Not only gross attacks upon the environment, such as cutting down trees, building houses, steering motor cars, etc., are mediated by the voluntary muscles, but also the communication of the most subtle shades of thought from one person to another. The activities of speech and writing, upon which all our communications depend, are highly co-ordinated muscular acts. If we go back one stage further these acts are the result of thought, and the material for thought is provided by the sense organs, some of which are very elaborate. The ramifications of their nerve fibres, and the connections in the nervous system which arise from them, are the complement on the sensory side of that part of the nervous system which is concerned with motor activity. We do not understand the nature of thought, but from the physiological point of view it is clear that *the activities of the body, in-so-far as it is not concerned in maintaining its own internal equilibrium, are directed to the mental and physical organisation and manipulation of the impressions which pour into it from the outside world. The expression of this activity depends on the voluntary muscles.*

CHAPTER VIII

THE CIRCULATION OF THE BLOOD

We have not devoted much space to describing what exactly blood is. It plays such a large part in every kind of activity that it is easier to consider its properties individually as they occur in relation to particular organs or systems. We have already mentioned that it has solid elements (the blood corpuscles) suspended in it and that they occupy approximately half of its volume, but for the purpose of discussing the circulation we may regard it simply as a fluid.

We are already in a position to appreciate the importance of the circulation and we must now describe how the blood is carried to the capillaries and how it is diverted to that part of the capillary circulation where it is most needed.

There is no beginning and no end to the circulation. It consists of a closed system of vessels of very different diameters. The capillaries are very small and very numerous but they arise by branching from larger vessels (arteries) and they re-join to form other large vessels (veins). The veins take the blood back to the heart where it is pumped out again into the arteries. So long as the pump keeps working, the blood keeps circulating.

This idea is obviously very easy to grasp, but it is equally easy to lose sight of it on account of certain minor complications. The most important of these is that once in every cycle the whole of the blood *must* pass through the lungs and as the blood vessels break up in the lungs into an extensive capillary system, the progress of the circulation is slowed down by friction and has insufficient force behind it to drive it through the remaining and more extensive capillary system of the rest of the body. After passing through the lungs, therefore, it is collected again into a second series of veins which lead to another pump, whence it is thrown into the arteries, which do finally convey the blood to the tissues in general. This is made much clearer in fig. 55, where it can be seen that the circulation is kept going allow the passage of blood in the forward direction only and strongly resist any back pressure. The outlet of the ventricle leads to the arterial system and is also closed by valves (fig. 57). These allow blood to pass in the outward direction but prevent it from running backwards from the arteries into the ventricle. The blood in the arteries is already at pressure and is thrusting back on these valves, so that considerable effort on the part of the ventricular muscle is required to open them and force more blood into the already distended arterial system. Directly the ventricle has forced its quantum of blood out into the arteries it relaxes and allows more blood to flow in from the atrium. The latter then contracts to distend the slack ventricle completely, and the cycle is repeated.

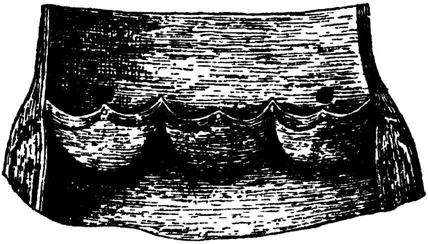

FIG. 57. Root of the aorta cut open to show the three semilunar valves. The two black dots are the openings of the coronary arteries which supply the heart with blood.

The regulation of the heart output

The muscle of the heart has the inherent property of shortening and lengthening rhythmically, so that the heart of an animal will continue to beat outside the body for many hours if precautions are taken to delay the death of its constituent cells. Although endowed with this fundamental rhythmicity, the organ would not be functionally so effective if it were not for a small collection of cells rather different from the rest of the heart muscle, the sino-auricular or " S-A " node (fig. 58), which is placed in the right atrium near the entrance of the great veins. It is possessed of a rhythm faster than all the other parts of the heart, and since these *can* beat at a rate exceeding their own fundamental frequency if stimuli are applied to them, the S-A node " drives " the heart at its own rate. The rhythmic excitation spreads from it first to the adjacent muscle and this passes it on to the fibres next adjacent and so forth. Fig. 56 shows that although this " milks " the blood out of the right atrium, the wave of excitation would reach the base of the ventricles the fraction of a second before the apex, and the latter would be subjected to considerable pressure while it was yet in the relaxed condition. This mechanical defect does not actually exist in the mammalian heart, because the ventricular muscle is separated by inactive fibrous tissue from atrial muscle in all but one place. At this place, the gap is bridged by a bundle of rapidly conducting tissue which resembles heart muscle in some details of its appearance and differs from it in others. It breaks up into branches and finally merges into a network of rapidly conducting fibres lining and penetrating the main mass of muscle. Fig. 58 makes the arrangement clear. The bundle starts in a node—

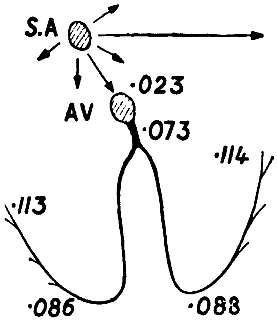

FIG. 58. Transmission of excitation in the heart.

S.A., sino-auricular node. A.V., auriculo-ventricular node. The rest of the diagram shows the auriculo-ventricular bundle and its branches The figures indicate the interval in seconds between the origin of a burst of excitation in the sino-auricular node and its arrival at various points in the heart.

the auriculo-ventricular or " A-V " node, similar to the S-A node, but at the lower edge of the right atrium, where it picks up the excitation from the atrial muscle. It transmits the excitation almost instantaneously to all parts of the ventricles, though it will be noticed that, apart from the wall between the two ventricles, the apex must contract before the base, where all the openings are situated. The intraventricular pressure rises steeply and the blood is thrust against the valves. Those between the atria and the ventricles are enabled to withstand the strain by strong tendinous fibres, not shown in the diagrams, which anchor them to the interior of the ventricles, and prevent them from being pushed inside-out. The valves between the ventricles and their respective great arteries are opened as soon as the ventricular pressure exceeds the arterial (see the next section) and blood is forced into the aorta and pulmonary artery.

The natural rhythm of the S-A node can be speeded up or slowed down by the action of nerves which are actuated reflexly (fig. 59). (The actual muscle of the heart also receives nerve fibres from the same sources which probably influence the strength of its contraction, etc.) The reflexes are a type of stretch reflex, the receptor organs being in two situations (1) the right atrium, i.e. on the receiving side, (2) in the aorta and the arteries

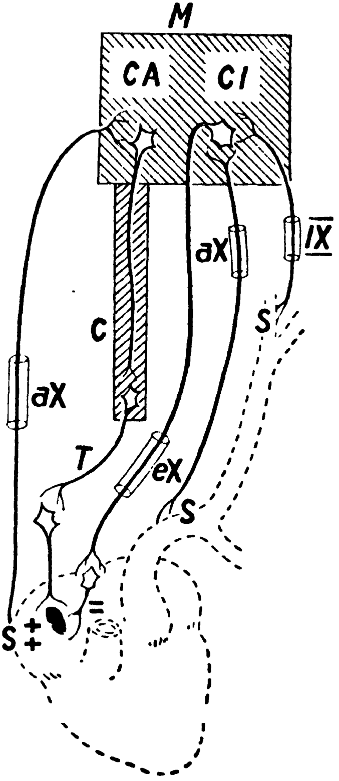

FIG. 59. Reflex control of the heart.

S, stretch receptors in right atrium, aorta and carotid artery. aX, afferent fibres of vagus nerve (tenth cranial). IX, afferent fibres in ninth cranial nerve. CA, cardio-accelerator, and CI, cardio-inhibitory, centres of the medulla, M. eX, efferent fibre of vagus. T, efferent fibre of sympathetic from spinal cord, C. The S–A node is shown as a black spot, and the action on it of the efferent fibres indicated by signs.

to the head (carotids), i.e. on the emitting side. The afferent path from (1) runs in the Xth cranial nerve (fig. 59) to the *cardio-accelerator centre* in the brain stem. The efferent path runs from here through the brain stem to cells in the upper part of the spinal cord, which are excited. The axons of these cells leave the cord as sympathetic fibres (fig. 56) which proceed via yet another relay station in a sympathetic ganglion to the heart, whose rhythm is speeded up. The effect of this is to get rid of the excessive amount of blood which is distending the right atrium, thus enabling the circulation rate to be increased.

The afferent paths from (2) run in the IXth and Xth nerves to the *cardio-inhibitory centre* in the brain stem. The efferent path in this case immediately leaves the central nervous system in those fibres of the Xth nerve which go to the heart. The frequency of the heart beat is reduced. The effect of this reflex is to protect the arteries from having so much blood delivered to them that they become over-stretched.

The blood vessels

The left side of the heart throws blood into the *aorta*, which is the largest artery in the body and the channel through which all blood must go before being distributed to the tissues. The walls of the aorta, which is about an inch in diameter, are thick and very elastic. The amount of blood which the ventricle pushes into it at every beat is often said to be about 60 cc., but may sometimes be much more than this. Now the contraction of the ventricle takes less than one-third of a second, so the aorta has to accommodate the blood almost instantaneously. The pressure within it rises to about 120 mm. of mercury (see p. 128) and its wall is stretched. The rebound of the elastic wall is slow and steady and forces the blood forwards into the branches of the arterial tree and so through the capillaries into the veins. The rebound is not exhausted by the time the next heart beat occurs and once more distends the aorta. The effect of this arrangement is to convert the individual " packets " of blood ejected at each beat of the heart into a flow which is continuous though not quite steady. In the normal individual the pressure in the aorta and its larger branches never drops below about 80 mm. of mercury, and its diameter is therefore never so small as that found on dissection after death.

If the small arteries and capillaries offered very little frictional resistance to the flow of blood, the latter would pass through them in waves, each wave corresponding to a heart beat. On the other hand, if their frictional resistance were very greatly increased then the aorta and large arteries would become more and more distended, and the pressure within them would rise until it was sufficient to force the blood steadily through the resistance. The diameters of the smallest arteries or *arterioles* are, in fact, variable and determined by the degree of contraction of the muscle in their walls, but they are sufficiently small to keep the arterial pressure above 80 mm. of mercury and the flow continuous (fig. 60).

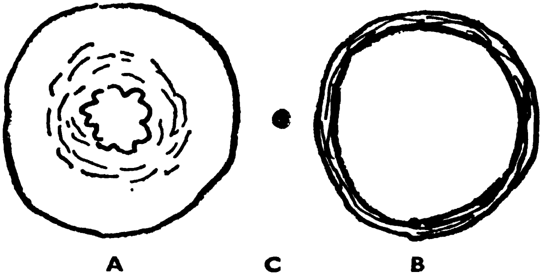

FIG. 60.

A shows the relation between the thickness of the wall and the bore of a small artery. It is magnified to the diameter of the aorta, B, whose wall is much thinner in comparison with its bore. The actual diameter of the small artery would be less than that of the dot C in comparison with the real diameter of the aorta (about 1 inch).

This muscle is of the smooth or involuntary type, the fibres arranged ring-like round the vessel (fig. 17). The fibres have the property of being able to assume different lengths and to maintain them indefinitely. The degree of contraction of smooth muscle at any time is often referred to as its " tone ". Smooth muscle also has the property of rhythmic contraction and relaxation, but its tonic contraction is much more important in blood vessels and it seems probable that this property has been developed in this situation at the expense of the power of rhythmic contraction. An arteriole is a very small blood vessel indeed and can be seen only under a microscope but its bore is larger than that of a capillary and its walls are very thick. In fact, in proportion to its diameter they are much thicker than those of the large arteries (fig. 60). The important difference is that the thickness is due almost entirely to smooth muscle rather than to elastic tissue. The muscle is supplied by nerves which run from sympathetic ganglia, and the nerve cells in these ganglia are in turn under the control of neurones whose cell bodies are in the spinal cord. These neurones are co-ordinated by a centre in the brain stem and this itself is probably under the influence of higher centres in the hypothalamus and even in the cortex itself. The latter probably plays very little part in the minute-to-minute routine adjustment of vascular tone, but it is well known that certain associations of ideas may cause the cheeks to become pale or to blush, and such changes of colour are an indication of the diameters of the underlying blood vessels.

Most blood vessels are also supplied by nerve fibres which convey impulses causing the muscle in their walls to relax. These fibres originate in various parts of the nervous system, but a great many of them appear to pass out through the *posterior* nerve roots and furnish the sole exception to the rule that these roots contain only those fibres conveying impulses *into* the spinal cord.

It is a demonstable fact that if a large proportion of the arterioles of the body constrict, then the pressure of blood in the large arteries rises and in extreme cases may be doubled. Conversely, if they are dilated the arterial blood pressure falls and the large arteries are much less distended. General rises and falls of blood pressure have a special significance to which we shall return shortly, but the chief purpose of this mechanism of control over the diameter of blood vessels is to divert blood from one part of the body to another. For instance, if several groups of voluntary muscle are working very hard, their arterioles are dilated and blood is passing easily and in large volumes through them, but arterioles in other parts of the body are constricted so that blood can only pass through them with great difficulty. This maintains the average head of arterial pressure, and the result is that very much more blood flows through the active tissues in a given length of time than would have done had the diameter of the arterioles remained constant.

The arterial blood pressure is not entirely dependent upon the diameter of the arterioles. Other things being equal, the frequency of the heart beat and the volume of blood which is ejected at each beat must have a profound influence. The more blood the heart puts out in a given time, the higher the arterial pressure will be and vice versa. Its output is controlled by the nervous system just as is the diameter of the arterioles and the two work in harmony (see p. 119).

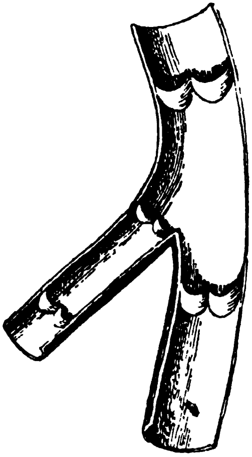

FIG. 61.
Vein cut open to show the valves.

The veins (fig.61) have such thin fibrous walls that they collapse when empty. They do not have to withstand high pressures, and are relatively deficient in muscle and elastic tissue.

The circulation in different localities

(*a*) *The brain.* The blood vessels of the brain are peculiar in having very little direct nervous control, and they therefore represent a certain fixed resistance. If the general arterial blood pressure is steady, the blood will be forced through them at a definite rate, but if the blood pressure falls the rate will become less and if it rises the rate will increase. Now since the arterial blood pressure depends (*a*) on the *total* frictional resistance and (*b*) on the output of the heart, it follows that the oxygen supply to the brain is depending on what is happening to the circulation in other parts of the body. If arterioles and capillaries elsewhere are too widely dilated then the effect on the cerebral circulation may cause unconsciousness (fainting). If general vasoconstriction occurs the pressure in the brain may become so high, especially in old people, as to burst a tiny blood vessel and cause a destructive release of blood into the substance of the brain. The general arterial blood pressure is, however, kept fairly constant, and in healthy people does not often fall below 100 or rise above 150 mm. of mercury. The stretch receptor organs in the carotid arteries may be regarded as outposts of the brain, which they protect by regulating the pressure of blood in these two vessels supplying it.

(*b*) *The heart.* It must never be forgotten that the heart itself is composed of muscle which needs to have an unfailing blood supply. The blood may not be able to pass quite so smoothly through the heart muscle as it does through other parts of the

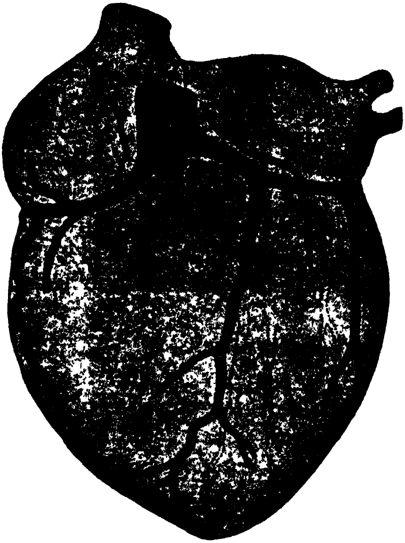

FIG. 62. The blood supply to the heart.

A, root of aorta with coronary arteries in black branching from it. The dotted lines represent their distribution on the other side of the heart. R.A., right atrium. L.A., left atrium. P.A., pulmonary artery.

body, because the channels in which it runs are alternately squeezed and released at every heart beat, but the supply is nevertheless of paramount importance. If the heart stops the whole body is deprived of oxygen. The heart is supplied by arteries which leave the aorta as it emerges from the ventricle (fig. 62). Their openings are just beyond the valves (fig. 57) and the flow of blood through them, like that through the brain, depends on the general arterial blood pressure. However, unlike the arteries of the brain, their walls *can* relax when the heart is very active, and *provided the blood pressure does not fall* this ensures an increased blood supply to the heart muscle.

(*c*) *The muscles.* The clause in italics raises a point to which we have referred previously, but which is most important in connection with a tissue of widespread occurrence like voluntary muscle. Suppose that during muscular activity the vessels of the muscles dilate, then, so long as the arterial pressure is maintained, they will receive a more copious supply of blood. But the muscles account for nearly half the weight of the body and if they were all working together they could accommodate an enormous quantity of blood. Now if the blood is in the arterioles and capillaries of the muscles it cannot at the same time be in the larger arteries, and as the latter close down on their diminished content of fluid, their walls are no longer passively stretched and the blood pressure must fall. This will reduce the rate of flow, and the circulation as a whole will tend to stagnate. In other words, the muscles, although full of blood, will not be getting the turnover they require. The blood supply to the brain and heart will also be endangered. It is observed that no disaster in fact occurs, and the reason is that other arterioles, for instance, those controlling the blood flow to the abdominal viscera, constrict so as to oppose a considerable resistance to the flow of blood, and by keeping the quantity in the viscera down to a minimum enable the stretch of the large arteries to be maintained.

When muscular activity is widespread, a great deal of heat is produced, and for this to be eliminated a large skin circulation is necessary. A mere redistribution of blood would be insufficient to enable a combined increase of circulation in both muscles and skin, but it is not the only mechanism. The heart rate may be speeded up enormously and blood delivered into the large arteries at such a rate that the pressure within them is maintained even though the frictional resistance is less than usual. The redistribution of blood is effected by the co-ordinating centres in the brain stem. The heart rate is increased by the activity of the cardio-accelerator centre (see p. 119) in the brain stem which is sensitive to nerve impulses which arise in stretch receptors in the right atrium of the heart. The flow of blood through the muscles is reinforced by the action of the muscles themselves, because their alternating contractions and relaxations compress the veins which run in and around them, and these veins are fitted with valves (fig. 61) so that when they are squeezed the blood is pushed forwards. This, combined with the driving force of the left ventricle, ensures the prompt return to the heart of the blood which has been thrown out and the response of the stretch receptors in the right atrium (p. 119) ensures that no obstructive piling up of blood occurs.

The difficulties in giving a complete mental picture of this process are usually underestimated. The reader labours under the obvious difficulty of not quite seeing how the whole process starts and gradually builds up.

It is probable that the very first incident is the production of an increased amount of waste products by the muscle which act chemically on the walls of the capillaries. Exposure of small blood vessels to an increased concentration of carbon dioxide is known to make them relax. In this way a fall of blood pressure is *threatened* and redistribution of vascular tone and increased heart rate follow to prevent this. When we deal with the ductless glands and the suprarenal in particular we shall be able to fill in some gaps in our present knowledge of this process.

(*d*) *The abdominal viscera.* A large proportion of the whole blood of the body is contained in the viscera. This word refers to all internal organs contained in the cavities of the body, e.g., the brain in the cranial cavity, the heart and lungs in the thoracic cavity, the liver, spleen, kidneys and intestines in the abdominal cavity, etc. During digestion the blood must supply the fluid and other components of the digestive juices, and also the oxygen and foodstuffs necessary for muscular contraction. The maximum amount of circulation in this region is needed during digestion and we often rest after meals, thus allowing blood to be diverted from the skeletal muscles. One abdominal organ worthy of special mention is the spleen (fig. 53). Its special function is to break up and deal with old red blood cells, but it also acts as a reservoir of blood and when the need of other parts of the body for blood is acute it may contract, and, like a sponge, squeeze blood out of itself into the circulation.

This brings us to the third factor in the control of blood pressure and the regulation of the circulation, namely, the total volume of circulating blood. It must be clear from what we have said previously that the arterial blood pressure depends on the relationship between the volume of the vascular system and the volume of blood. We have seen that the volume of the different parts of the vascular system can be changed and that if it increases in one place then the heart and other vessels must compensate. Another kind of compensation would be to increase the total volume of blood and such compensation is made to a limited extent by the spleen.

The main peculiarity of the circulation in the abdomen is that the *portal vein*, which collects all the blood from the digestive tract and spleen, does not join up with the other large veins which are making for the heart. Instead, it leads into the *liver* (fig. 53), where it divides and subdivides into a completely fresh capillary system. This is not so much for the sake of the liver, which has its own artery supplying it with oxygenated blood from the aorta, as for the benefit of the rest of the body. The blood from the digestive organs is laden with food, and this arrangement of the vascular system enables it to be dealt with immediately by the liver, which is the great chemical workshop of the body. The blood which enters the liver by the portal vein and that which goes in by the ordinary arterial route leave as a mixed stream which then joins the blood from the rest of the lower part of the body to enter the heart.

CHAPTER IX

THE SOURCE, TRANSPORT AND SUPPLY OF OXYGEN

THE source of oxygen is the atmosphere, of which it comprises about one-fifth by volume. It is important to realise, however, that the rate at which oxygen passes from the atmosphere into any fluid and into the blood depends on the *pressure* which it exerts.

It is well known that the atmosphere at sea level has a definite pressure owing to the weight of all the layers of atmosphere above it. This pressure is usually measured in terms of millimetres of mercury. Mercury is used because it is a very heavy liquid. If we have a long tube closed at one end and shaped like an inverted U, and we fill the closed limb with mercury, we have the state of affairs depicted in fig. 63*a*. If now we turn the U the right way up, taking care that no bubbles of air pass up into the top end, we shall have the state of affairs shown in fig. 63*b*. The space which has appeared between the closed end of the tube and the surface of the mercury is a vacuum. Although it is not obvious at first this arrangement is a kind of balance. Standing on top of the open surface of the mercury is a column of air which reaches right up into the stratosphere and beyond. The weight of this air tends to push the mercury from right to left round the U. On the surface of the mercury under the closed tube there is no pressure. It is protected from the atmosphere by the closed end, and between this and the surface of the tube there is no material at all. Since the mercury is stationary it is clear that the weights acting on the U on each side of the point A are equal. If we draw a horizontal line at the

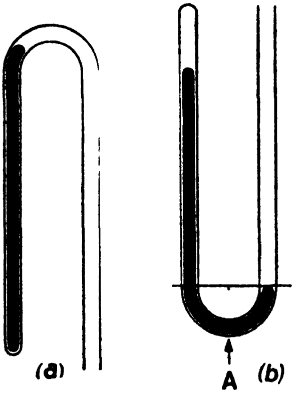

FIG. 63. To illustrate the measurement of pressures in terms of mm. of mercury (see text for explanation).

surface of the mercury in the short limb so that it passes through the mercury in the long limb, we have the same weight of mercury on each side of A *below* this line, and we are left with the observation that the weight of mercury in the long limb above this line must be equal to the weight of the column of atmosphere supported on the surface of mercury in the short limb. This would be true whatever the diameter of the tube and when we say that the atmospheric pressure is approximately 760 mm. of mercury, we mean that a column of atmosphere at the point where we are working would support a vertical column of mercury 760 mm. high.

The atmospheric pressure varies from day to day, but in order to make rough calculations it is useful to refer always to the "normal" pressure of 760 mm. of mercury. If this is the total atmospheric pressure, then that part of it for which oxygen is responsible is 152 mm. or 1/5th of the total. Carbon dioxide occupies only 0.04 per cent of the atmosphere, so its share of the pressure—or its partial pressure to use the correct term—is only about 0.23 mm. of mercury, which is negligible. Nitrogen and the remaining inert gases of the atmosphere account for the difference of about 518 mm. of mercury. These calculations would be true for absolutely dry air, but the atmosphere is never quite dry and contains a variable amount of water vapour. It the air were fully saturated with water vapour, as on a foggy day, the pressure exerted by the water vapour might be about 14 mm. of mercury at ordinary temperatures (e.g. 60°F).

It happens that the methods for analysing the composition of atmospheric air take no account of water vapour. What they really reveal is the composition by volume of the air *excluding* water vapour. At a barometric pressure of 760 mm. of mercury, therefore, we should first subtract the pressure of the water vapour, and then calculate the partial pressures of the remaining gases. It will be seen that even if atmospheric air at about 60°F. is fully saturated with moisture, our correction makes a relatively small difference. Subtracting 14 mm. of mercury for water vapour leaves us with 746 mm., of which 149 are due to oxygen, and the remainder to the inert gases with a trace of carbon dioxide.

In the depth of the lungs the water vapour occupies a much greater volume, because the temperature is 37°C. and the air is in contact with an immense moist surface (warm air can accommodate much greater quantities of moisture than cold air). The pressure then exerted by the water vapour is 47 mm. of mercury, leaving only 713 mm. to be shared between oxygen, carbon dioxide, and the inert gases. Moreover, we find that the percentage of carbon dioxide is much greater here than in atmospheric air and the percentage of oxygen correspondingly smaller, so that for a typical composition of 5.5 per cent carbon dioxide, 14.5 per cent oxygen, and 80 per cent nitrogen, the partial pressures are as follows:—

Water vapour	47	mm. of mercury
Oxygen	103	,, ,, ,,
Carbon dioxide	39	,, ,, ,,
Nitrogen	571	,, ,, ,,

It cannot be too strongly emphasised that, although the composition of alveolar air is always of this order, it varies from individual to individual and slightly in the same individual from moment to moment.

The important conclusion to be drawn from these facts is that blood leaves the lungs to go to all other parts of the body having been in contact with a pressure of oxygen of over 100 mm. of mercury and with carbon dioxide at a pressure of about 39 mm. of mercury. It is much more difficult to assess the pressures of these gases which the blood encounters in the tissues. We know that the cells of the body are using oxygen and therefore the fluid which immediately surrounds them will be continuously depleted of the oxygen dissolved in it, and molecules of oxygen will move towards it from more remote portions of fluid and ultimately from the blood plasma itself. It is very doubtful to what actual pressure of oxygen the activity of the tissues corresponds. Clearly, the harder they work and the more oxidation of foodstuffs they perform, the lower this pressure will be and the steeper will be the gradient of "suction" of oxygen from blood to cells.

Oxidation involves the production of carbon dioxide, so we know that the pressure of this in the tissues will rise and there will be a positive gradient from tissues to blood. The actual distances over which these gradients operate are very small, particularly in organs addicted to hard work, because they are so richly supplied with capillaries. We may, in fact, regard the blood as passing through a kind of " atmosphere " in which the pressure of oxygen is less (perhaps half) that in the lungs, and the pressure of carbon dioxide is greater (perhaps 50 mm. of mercury). These figures vary in opposite directions with the degree of activity of the tissues in various localities. The amounts of oxygen and carbon dioxide in the mixed blood entering the lungs represent the resultant of all the different " atmospheres " through which the various batches of blood from arms, legs, abdomen, etc., have passed.

In watery fluids like those which permeate the body, the amount of a gas, such as oxygen or carbon dioxide, which will go into solution at these pressures is quite small. The blood is peculiar in being able to take up or release unusually large quantities of these gases when the pressures they exert are slightly changed. It will be seen from fig. 64 (*line A*) that the amount of additional gas which is forced into ordinary

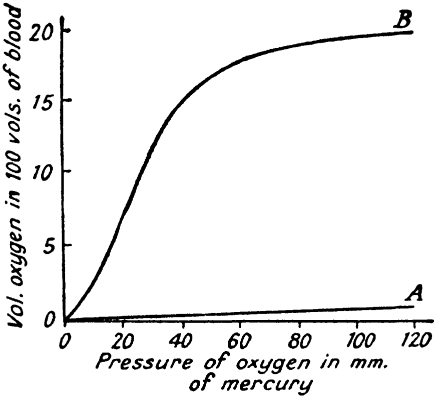

FIG. 64. Line A shows the volume of oxygen taken up by 100 vols. of water, and line B the volume of oxygen taken up by 100 c.c. of blood on exposure to various pressures of oxygen.

solution is directly proportional to its change of pressure; for each mm. of mercury of increased pressure a certain volume is dissolved, and for every mm. of mercury of decrease the same volume is liberated. Blood does not obey a simple law in this respect. It starts by taking up a certain volume of oxygen for each mm. rise in oxygen pressure, this volume steadily increases until it becomes large and finally begins to diminish again (fig. 64 *line B*). By the time the pressure of oxygen has reached 100 mm. of mercury, the additional volume being absorbed for even large rises of pressure is very small. The blood is then said to be " saturated " with oxygen. When human blood is saturated it contains about twenty volumes of oxygen in every 100 vols. of blood, instead of the mere 0.36 vols. it would have been able to accommodate if it had relied on the solubility of oxygen in its fluid component.

The substance responsible for the additional oxygen capacity of the blood is *haemoglobin,* the pigment in the red blood corpuscles. The oxygen does not dissolve in the haemoglobin nor yet is it firmly united to it in a definite proportion as it would be were the haemoglobin oxidised in the chemical sense. The way in which oxygen is held is not fully understood. It is known, however, that the amount of oxygen which haemoglobin can take up depends on the pressure of this gas to which it is exposed, and although the process of oxygen absorption is obviously different from that of pure solution, its course can easily be followed. A given quantity of blood can be placed in each of a series of air-tight vessels, and an artificial atmosphere created in each vessel, ranging from pure nitrogen to pure oxygen with various mixtures in between. (The nitrogen has no effect except to reduce, by an amount proportional to the volume it occupies, the partial pressure of oxygen.) After having been thoroughly exposed to these atmospheres, the samples of blood can be transferred, taking care not to let them come into contact with air on the way, to an apparatus capable of extracting and measuring all the oxygen which they contain. For each of the original vessels we can then make the statement that so many cc. of blood having been exposed to such and such a pressure of oxygen contain so many cc. of oxygen. It is usual to plot the results in the form of a graph (fig. 64) showing the volume of oxygen which would be contained by 100 cc. of blood at each of the pressures of oxygen to which it was exposed. On an average 100 cc. of blood is saturated when it contains about 20 cc. of oxygen and it attains this condition shortly after the partial pressure of oxygen passes 100 mm. of mercury. Saturation therefore occurs in the lungs, where, as we have seen, the pressure of oxygen is more than 100 mm. of mercury.

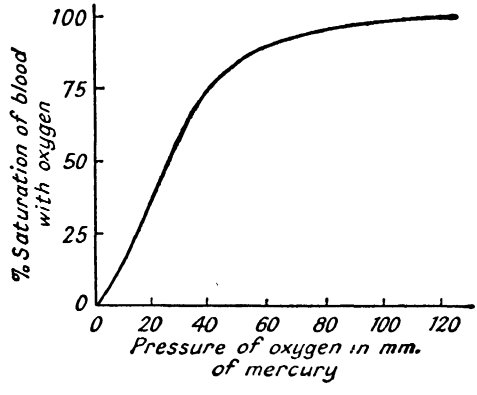

FIG. 65. The amount of oxygen taken up by blood at various pressures is expressed as a percentage of the maximum volume which the sample of blood being examined is capable of accepting.

If we are investigating the condition of the arterial blood in a diseased person whose blood is not fully saturated when it leaves the lungs, we can if we like state how many cc. of oxygen 100 cc. of his blood contains. But the oxygen content of his blood is very rarely expressed in this way because it is much more important to know what relation it bears to the amount he *could* carry, i.e. the total capacity of *his* blood for oxygen

If a person has only half the number of red cells, and, therefore, only half the amount of haemoglobin which a normal person has, then the oxygen content of his arterial blood will be correspondingly low, even if it is fully saturated. Another person may be carrying no more oxygen, but he may possess the normal amount of haemoglobin, in which case his blood is only "half saturated". Quite apart from these extreme cases, the total oxygen capacity of the blood of different people varies somewhat according to their haemoglobin content, and it is often more convenient to speak of the oxygen content of blood in terms of *percentage saturation*, than in terms of actual volumes per 100 cc. The ***oxygen dissociation curve*** (fig. 64 *line B*) is, therefore, frequently found in the form shown in fig. 65, where percentage saturation instead of volumes of oxygen per 100 cc. is plotted against pressure. For "normal" blood, approximately 20

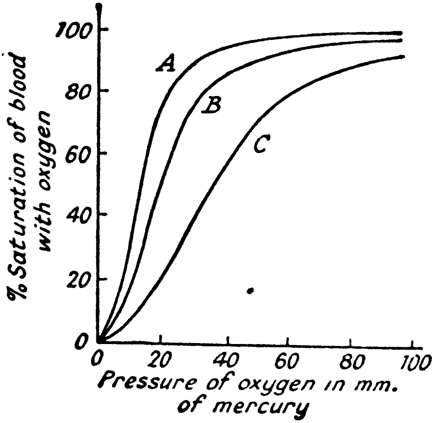

FIG. 66. The effect of carbon dioxide on the shape of the oxygen dissociation curve of blood.

A was constructed throughout at a pressure of 3 mm. of mercury, B at 20 mm. mercury, and C at 90 mm. mercury of carbon dioxide. (Barcroft and Poulton, *J. Physiol.*, Vol. 46.)

volumes per cent equals 100 per cent saturation, but fig. 65 has the advantage that it can be applied to solutions of haemoglobin in any concentration, and will still give a true picture of the behaviour of haemoglobin on exposure to oxygen.

The behaviour of haemoglobin is altered somewhat by the presence of carbon dioxide in the blood. In fig. 66, *A* is a typical oxygen dissociation curve for blood which contains very little carbon dioxide, *B* for blood which contains more carbon dioxide, and *C* for blood which contains rather a lot of carbon dioxide. The blood of any one person, therefore, can be made to yield several oxygen dissociation curves by the simple expedient of submitting it to a series of exposures each covering the full range of oxygen pressures, but the air mixtures in any range differing from those in another range in the amount of carbon dioxide they contain.

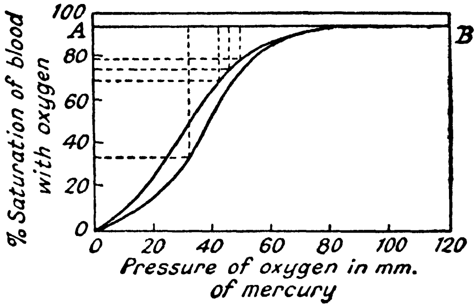

FIG. 67.

The level of the line AB indicates the oxygen saturation of arterial blood in a certain person The levels of the dotted lines from above downwards represent the oxygen saturation of his venous blood when lying, sitting, standing and undergoing exercise. The positions of the vertical lines indicate the pressure of oxygen to which the blood has been exposed in the tissues. During exercise the blood contains more carbon dioxide than usual, and the corresponding shift of the dissociation curve to the right is shown. It means that the blood parts more readily, i.e. at a higher pressure, with its oxygen (Y. Henderson, *Lancet*, 1925.)

Fig. 67 shows how beneficial this property of carbon dioxide can be. In the muscles, where the pressure of carbon dioxide is high (and that of oxygen low), the blood obeys the right-hand dissociation curve. In the lungs, where the carbon dioxide pressure is low (and that of oxygen high), it obeys the left-hand curve. The net result is the maximum change of oxygen content with the minimum change of oxygen pressure.

CHAPTER X

CARBON DIOXIDE

THE way in which carbon dioxide is carried by the blood is too complicated to explain in this book. Part of it is carried by direct combination with haemoglobin, but most of it is accommodated in a quite different way by a chain of easily reversible chemical reactions which culminate in forming sodium bicarbonate. Chemists will understand that the " bicarbonate " half of this molecule contains what was originally carbon dioxide, while the sodium part has been made available by the release of sodium (or its equivalent, potassium) from combination with the large protein molecules of the blood—haemoglobin and plasma proteins. The amount of bicarbonate (representing a certain volume of carbon dioxide) which is contained in any sample of blood depends on the pressure of carbon dioxide to which it is exposed. In ordinary water exposed to a certain pressure of carbon dioxide and therefore accepting a certain volume into simple solution, an increase of pressure forces another increment of carbon dioxide into solution and there the matter rests. In blood, most of this increment is readily converted into bicarbonate, and what might be visualised as the vacant space in the solution is, of course, promptly filled up by more carbon dioxide, of which most again is converted into bicarbonate. This goes on only until the blood plasma will accept no more carbon dioxide into simple solution. But at this point it has aready accepted about twenty times as much carbon dioxide as ordinary water would have done (fig. 68). It is a pity we cannot go into this matter fully because it is important. However it will suffice for our purpose if we realise that while the blood is extraordinary chiefly because of the *large quantity of carbon dioxide which it can readily accept or release* when the pressure of carbon dioxide is changed, the *small quantity of carbon dioxide simply dissolved* in the plasma also has important functions. A brief digression on this point will not be out of place.

We had a good deal to say in an earlier chapter about the constancy of the internal environment of the body. One of the most important quantities which must be kept constant is the concentration of hydrogen ions. A hydrogen ion is a special form of hydrogen atom found in solutions of certain hydrogen compounds. The hydrogen used for filling balloons is really a collection of *molecules* of hydrogen, and each molecule is a compound of two atoms. However, when acids are dissolved in water, the hydrogen which was part of the molecule very often becomes "semi-detached". It has a certain degree of freedom from the parent compound, which it keeps leaving and joining again, darting about in the solution and changing places with its fellows. If we could see into such a solution at any moment a certain number of these hydrogen ions would be on their way from one molecule to another, while a certain number would be joined up to their molecules. Different substances behave in different ways. In some the exchange is so free that, at any instant, the majority of hydrogen ions are on the move. These substances are strong acids. In others (weak acids) relatively few hydrogen ions are on the move, and most of them are resting quietly in combination with the parent molecule.

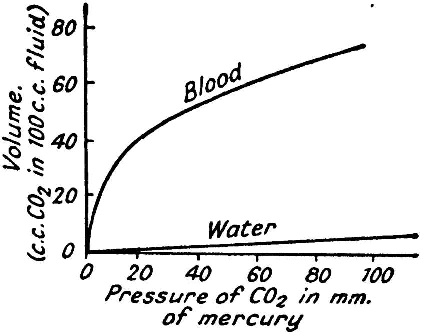

FIG. 68. To show the volumes of carbon dioxide accepted by blood and water respectively at various pressures.

Part of the total accepted by blood is in simple solution as it would be in water, and the ratio between simply dissolved and chemically combined fractions is important.

Exactly similar considerations apply to what are known as "hydroxyl ions". These are each a combination of one atom of hydrogen with one atom of oxygen. This combination

" hydroxyl " resembles the hydrogen ion in being unable to exist alone in the absolutely free state and in occurring only in a modified state of freedom, when it can be semi-detached in solution from a larger molecule. When hydrogen ions and hydroxyl ions meet, as they do when compounds containing them are dissolved in the same sample of water, they combine firmly together to form water itself, and are thus suddenly transformed from being very active components of the substances dissolved into a stable compound which is itself the dissolving substance —water. Substances liberating hydroxyl ions are called alkalies, and, on account of the occurrence we have described, alkalies and acids neutralise each other.

Even the purest water contains a very small, but equal, concentration of hydrogen and hydroxyl ions. That is to say, water does possess in a very slight degree the property of giving a certain amount of freedom to its constituent ions, though nearly all of them are in a state of combination as water itself. It can now be appreciated that if water is slightly contaminated with acid, there will be a preponderance of free hydrogen ions and if it is slightly contaminated with alkali a preponderance of hydroxyl ions. Furthermore, if water like that of the blood plasma contains a great many substances in solution, the balance between hydrogen and hydroxyl ions will be unaffected only if none of the dissolved substances yield either ion. If some of them yield one and some another they will neutralise each other up to a point, but there may finally be a slight imbalance in one direction or another. In blood there is a slight excess of hydroxyl ions and this happens to be important. The chemical processes which go on in cells become very much impaired if the balance between hydrogen and hydroxyl ions is upset. The state of the balance can be expressed either in terms of the concentration of hydroxyl ions or that of hydrogen ions present at any time. In practice, although the hydroxyl ions in blood are in larger number, it is customary, for the sake of uniformity, to refer to the concentration of hydrogen ions.

Returning to our starting point, we must now take account of a new fact, namely, that when carbon dioxide is in simple solution it gives rise to hydrogen ions, whereas sodium bicarbonate in solution gives rise to hydroxyl ions. It is unfortunate that we cannot in this book explain the matter quite fully. Readers with some knowledge of chemistry will realise that neither carbon dioxide nor sodium bicarbonate actually contain these ions, but they will have to take the author's word for it that, by secondary reactions which they undergo with water, they do, in fact, very quickly give rise to them. The hydrogen ion concentration of blood is within normal limits when the amount of carbon dioxide in simple solution is about 1/20th of that combined as bicarbonate. During the changes incident on respiration, as we have stated before, this proportion which already exists in blood remains practically constant, because for every molecule of carbon dioxide which goes in or out of the simple solution, about 20 molecules go in or out of combination as bicarbonate. Unfortunately, this proportionality does not hold good over a wide range of concentrations, so that if we push an excessive amount of carbon dioxide into blood by exposing it to an abnormally high pressure of this gas, the proportion taken up as bicarbonate tends to drop, and the hydrogen ion concentration of the blood rises slightly. Similarly if an excessive amount of carbon dioxide is removed from the blood, rather more than 1/20th of the total amount is yielded at the expense of the carbon dioxide in simple solution, and the hydrogen ion concentration of the blood falls slightly. At no time is an actual preponderance of hydrogen over hydroxyl ions in the blood compatible with life, so the blood is never actually acid. But from the *directions* in which the above changes are tending, the conditions are sometimes called respectively acidosis and alkalosis.

When we breathe we are, therefore, not only enabling the blood to take up oxygen, but we are also protecting the body from accumulating too much carbon dioxide, which would raise its hydrogen ion concentration. The reason we have devoted so much space to giving a partial explanation of this point is because we now have to state a fact which otherwise might seem a very curious one. It is that *the nervous centres and their outlying sense organs controlling respiration are more sensitive to threatened changes in the hydrogen ion concentration of* *the blood than they are to a deficiency of oxygen in the blood.* In other words, respiration at sea level (or low altitudes) and under normal conditions of exercise and so forth is controlled by the pressure of carbon dioxide in the lungs and not by the pressure of oxygen. (In abnormal circumstances which nowadays are very common, e.g. at high altitudes, the pressure of oxygen is a very much more important factor.)

The fact can be demonstrated by a very simple experiment, but the reader is advised not to carry this out in solitude. If the nose is clipped so as to obviate unconscious " cheating ", and all breathing is done through the mouth in and out of a bag of a few litres capacity, two things will happen to the air inside the bag. Its oxygen content will be diminished and its carbon dioxide content will be increased. In a very short time, the subject of the experiment will begin to feel very breathless and his respiration will increase in depth and frequency. He will feel as though he was running at top speed and fighting for air. There is no danger in this part of the experiment because immediately the discomfort becomes too great, the bag will be thown away. If, however, a tin or a vessel containing " soda-lime " is inserted between the bag and the subject's mouth, so that the air he breathes passes back and forth through it, he will feel no discomfort for quite a long period. The reason for this is that while the amount of oxygen in the bag is diminishing, the carbon dioxide concentration is not rising, because the soda-lime absorbs this gas. A certain amount of breathlessness may be experienced after a time but many people do not notice it until the oxygen in the bag has sunk to dangerously low levels. When the danger point is approaching, their complexion and lips may assume a bluish tinge, and if the bag is not removed so that they can breathe ordinary air again, they may actually lose consciousness from lack of oxygen, having had practically no physical discomfort.

CHAPTER XI

THE RESPIRATORY TRACT

THE actual process of respiration has two aspects: (*a*) the utilisation of oxygen by the tissues, and (*b*) the uptake of oxygen and elimination of carbon dioxide in the lungs. In Chapter XII we shall discuss the control of the latter process, which has to be adjusted to the needs of the body. It will be apparent from what we have said in Chapter X that other factors besides the simple supply of oxygen are involved. Before turning to any of these problems we must consider briefly some features of the mechanical arrangements which are available for the transfer of gases between air and blood.

We have mentioned the profuse branching of the air passages, and this is shown diagrammatically in figs. 49 and 50. The general consequences of an arrangement like this are simple enough to understand. We have already pointed out that it enables air of a different composition from that of atmospheric air to be kept relatively stable in composition in the depths of the lungs, and we have also remarked on the enormous area of blood and air which are brought into very close contact by it. We shall, therefore, not elaborate this side of our investigation, but merely point out two or three features of the respiratory tract which are not obvious from its anatomical shape and the disposition of its parts.

(a) Protective devices

The inside of the air passage is moist, and loose particles are thereby prevented from floating about in the inspired air. In order to appreciate the significance of any structure whose function is not obvious, it is often amusing and instructive to work out the consequences of an alternative. If the inside of the air passages were lined with skin, like that on the surface of the body, they would still be quite efficient ducts for the carrying of air, but the external layers, like those of the skin, would flake off, and as the contiguity of blood and air in the depths could scarcely be brought about without the intervention of a moist surface, the debris would presumably stick here, and in the course of time obstruct the transfer of gases.

Not only does the moisture lining the tubes contain waste material broken off from the lining cells, but particles already in the inspired air adhere to it. It is a matter of common observation that this moisture film is sticky in character, which is due to its containing a substance, ***mucin***. The cells lining the trachea (windpipe) and its branches are columnar in shape, and many of them are seen to be distended with a blob of fluid. This is the solution of mucin which the cell is about to discharge to the exterior. It has been manufactured by the cell from constituents of the blood plasma and the process is termed *secretion*.

Another significant structural adaptation which is seen is that, for a considerable distance inwards, the columnar cells lining the respiratory tract bear hair-like structures, called cilia, which like smooth muscle are endowed with the inherent power of rhythmic movement. This movement is whip-like, and as all the cilia in one neighbourhood act in unison, mucus is swept upwards. If the lining of the throat of a recently killed frog

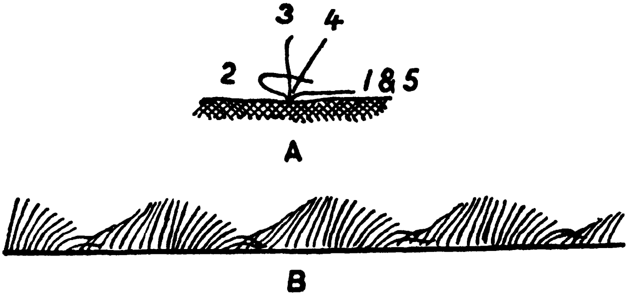

FIG. 69.

A. Successive stages in the movement of a single cilium sweeping material from left to right. Note how it straightens on the forward stroke.
B. A field of cilia in motion. They are all in different phases of the forward stroke.
(After T. C. Barnes, *Textbook of General Physiology*, Blakiston, 1937.)

be removed and pinned out on a board and small black particles, e.g. of charcoal, placed upon it, they will be seen to move under the influence of the action of cilia. The movement of single cilium is depicted in fig. 69*A* in its successive phases. If we take the respiratory tract as a whole, we find that all the cilia are not in the same phase of movement simultaneously. A wave of movement passes from below upwards in much the same way as a field of corn is moved by a gust of wind (fig 69*B*). The only difference is that in the case of cilia the movement is active and not passive, and the activity of the units is beautifully co-ordinated so as to produce the maximum speed of movement in any object which they are driving forwards.

A further protection against the inhalation of solid particles, particularly large ones which might not be so easily removed by cilia, is the extreme sensitiveness of the respiratory passages to irritation. This is too familiar to need description, and results in a cough or sneeze. Coughs and sneezes are really explosive ejections of air, which carry with them the offending foreign body together with some of the mucus. Coughs and sneezes are excellent examples of reflex action. The afferent path is the sensory nerve supplying the surface cells, and when the impulses which are set up reach the central nervous system, they give rise to a burst of activity on the part of the motoneurones supplying the muscles of the chest and abdomen, and a considerable weight of muscle is thrown into violent contraction. The discharge of excitation from the central nervous system is obviously much greater in quantity than the excitation it has received. It is clear that the motor centres in question are primed with excitation from controlling centres in the nervous system, and that the additional impulses from the air passages, by adding their quota, act as a kind of trigger which releases a great deal of energy. Some of the incoming impulses ascend high enough in the central nervous system to produce sensation, and, finally, movement may be reinforced by considerable voluntary effort.

Other obstructions to the entry of foreign bodies into the air passages are the hairs (vibrissae) inside the nose, and the complicated nature of the nasal passages themselves. The air here comes close to a quite large volume of blood, the vessels carrying which are arranged on a kind of sponge-work foundation. This blood has the effect of warming the air which is breathed in (fig. 70).

The foreign bodies we have so far mentioned range from those which are visible to those which can only be seen by a microscope, but there is yet another class, namely bacteria. The upper air passages, i.e. the neighbourhood of the back of the nose and throat, are lined with *lymphoid tissue*. Beneath the surface are millions of cells identical with one of the varieties to be found in the blood stream. They are the small white cells of the blood or *lymphocytes* (fig. 51). It is far from certain how they deal with bacteria, but they are known to be antagon-

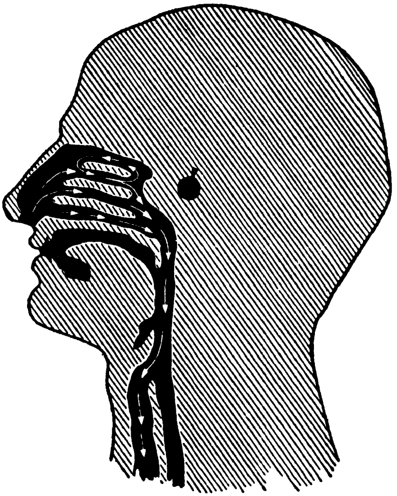

FIG. 70. The upper air passages.

The horizontal shelves subdividing the nose project from the outer wall of the cavity on each side, the centre wall or septum being flat. The tissues here are very vascular. Further back they are lined with lymphoid tissue. (The position of the pituitary gland is shown by a black spot for future reference. It is not concerned in respiration.)

istic to them and collections of them are found in various parts of the body, where they are so placed as to act as a barrier to infection. It would be very difficult to breathe through any sort of protective meshwork, but the local concentration of these cells in the upper respiratory tract is presumably the next best

The bronchial muscles do not, however, have any power of driving air backwards or forwards in the lungs. They represent a potential obstruction, and their partial contraction during expiration may have something to do with keeping the delicate culs-de-sac in which the tiniest air vessels end always distended. We do not know. The tubes are themselves kept open by rings of cartilage (gristle). Unfortunately, the muscles sometimes get out of control, and, by contracting excessively, narrow down the bronchi too much and produce the obstruction to breathing known as asthma. The conditions which bring about this over-action make a fascinating study, but are too complicated for us to discuss here.

(c) The alveolar membrane

The culs-de-sac in which the finest bronchial vessels end (fig. 49) are the place where the air and the blood come close together. They are made of the thinnest possible plate-like cells. On one surface is the network of blood vessels, and on the other a pocket of air. In some animals this membrane is deficient, and the only barrier between air and blood is the thin wall of the capillary blood vessels. The little terminal balloon is strengthened by a network of elastic connective tissue which becomes stretched when it is distended by inspiration. Although individually they are insignificant, collectively the elastic fibres are sufficient to ensure expiration without any aid from muscles. In fact, if the chest is opened and air admitted between the wall of the chest and the outside of the lung, the elastic tissue converts the lung from a structure filling half the chest to a lump of material no bigger than one's fist (fig. 71).

The barrier between air and haemoglobin may be regarded as a layer of fluid. The surface of the alveoli is moist, the thin plate-like cells and the cells of the capillary wall are mostly composed of water, and between them is a layer of tissue fluid. The diameter of the capillaries is little more than sufficient to accommodate one red cell. Since the latter are passed through these channels practically one at a time, the layer of plasma between capillary wall and red cell is inconsiderable. Finally there is the fluid of the red cell itself, in which the haemoglobin is dissolved. None of these fluid sub-divisions differs materially from water in its power to dissolve oxygen and carbon dioxide. The question naturally arises: of what benefit is the ability of haemoglobin to absorb large volumes of oxygen at low pressures when this barrier of low solubility is interposed between it and the source of the oxygen?

The answer to this question is simple but worth explaining at some length. If a volume of fluid exposed to a certain pressure of oxygen in a closed container has come into equilibrium with the oxygen, that is to say, if it has dissolved all the oxygen it is able to dissolve at that particular pressure, and it is then transferred without coming into contact with air to another vessel in which the partial pressure of oxygen is much less, then it will give up some of its dissolved oxygen. *The oxygen dissolved in the water itself exerts a pressure* which must always be equal to the pressure exerted upon it. If this equality is disturbed it restores itself immediately. Now we have said that the air in the depths of the lungs remains almost constant in composition, which means that the oxygen in the fluid layer in contact with it must be at a certain corresponding pressure. In the blood vessels is haemoglobin which has just come from the tissues, a region of low oxygen pressure, and it is surrounded by its own layer of fluid containing oxygen at this low pressure. When the two sheets of fluid, that in the blood and that in the lungs, meet to form the composite layer separating alveolar air and haemoglobin, we may picture the molecules of oxygen instantly distributing themselves so as to equalise the pressure of oxygen throughout the layer, which is then at a lower oxygen pressure than the alveolar air but at a higher one than the haemoglobin. There is again an instantaneous movement of the molecules from the regions of high to those of low pressure, and oxygen passes into the fluid from the air and out of the fluid into the haemoglobin. As the oxygen pressure of the alveolar air is maintained by breathing, the result is a rapid transfer of oxygen across the barrier until the pressure in the blood attains that of the alveolar air. These facts mean that the oxygen *content* of the fluid barrier does not matter, so long as a sufficient number of molecules of oxygen enter it on one side and leave it on the other to satisfy the volume of blood which passes through the lungs in a given time. It is like the pipe which connects the storage tank of a domestic hot water system to the boiler. The *volume* of water in the pipe does not matter so long as the pipe is wide enough to fill the boiler as quickly as water is taken from it, i.e. so long as the total volume passing *through* it in a given time is adequate.

The reader might ask at this point: What happens if the body is doing very hard work and the flow of blood through the lungs is extremely rapid? Is the speed with which the oxygen molecules travel across the fluid barrier still great enough to transfer the amount of oxygen which is needed in a given time? The answer is based on experience. Only in a very small number of people, whose lungs are probably abnormal, is it thought that the fluid barrier is the limiting factor in the speed with which oxygen can be taken up, but even in these individuals the limit is only encountered during strenuous exercise. (The rate at which oxygen can be supplied to the alveolar air by the act of breathing is never under normal conditions a limiting factor. We can always breathe fast enough. This naturally does not apply when the amount of oxygen in the atmosphere is deficient.)

In pneumonia fluid exudes from the capillaries into the lungs in considerable quantity and they become water-logged. The fluid barrier is now very thick and the passage of oxygen from air to blood is impeded. The condition is probably made worse by the fact that the fluid contains proteins which tend to clot into a semi-solid mass. In such circumstances it is obvious that raising the partial pressure of oxygen in the lungs, which can be done by giving the patient pure oxygen instead of air to breathe, will materially assist the uptake of oxygen by the blood because the speed with which oxygen molecules traverse the barrier is dependent upon the pressure difference between its two surfaces.

CHAPTER XII.

THE REGULATION OF RESPIRATION

THE actual mechanics of breathing are too simple to require more than a brief description. The branching structure of the respiratory tract completely fills the cavity of the chest, with the exception of the space taken up by the heart, the large blood vessels, and one or two other structures. Its volume depends on the volume of the chest and when this is enlarged, air is drawn into it. Except for one detail it is as if the outside surface of the lungs was actually attached to the wall of the chest. We must not be confused by the fact that on dissection the lungs can be handled as separate structures. During life there is no air between the smooth surface of the lungs and the smooth inside surface of the chest. The two are everywhere in contact. Anyone who has tried to separate two sheets of glass, moistened on their opposing surfaces, will understand that although the surfaces of the lungs and thorax can slide over each other (they are lubricated by a little fluid) they cannot be separated by direct traction, and so far as breathing is concerned they act as though they were attached, except that the sliding movement prevents the delicate structure of the lungs from being torn by the powerful expansion of the chest.

There are only two circumstances, both abnormal, in which the lungs can become separated from the chest wall. (*a*) In the disease of pluerisy, which is an inflammation of the sliding surfaces (the pleura), sufficient fluid may be exuded to make a considerable layer between them; (*b*) in certain diseases of the lungs or injury to the chest, air may leak between the two layers and the elastic tissue in the lungs which we described in the last chapter is then sufficient to cause the lungs to collapse and air to fill the space which now exists between their surface and the inside of the chest (fig. 71). The introduction of air (artificial pneumothorax) is sometimes performed in order to rest a lung which is diseased.

The expansion of the chest is brought about chiefly by movements of the dome-shaped diaphram which closes the bottom of the cage formed by the ribs, breast-bone and spinal column. It is composed of voluntary (striated) muscle whose fibres radiate from a central tendon to be inserted in the walls of the cage. When they simultaneously contract, the dome is flattened and the corresponding movement of the lungs with intake of air occurs. At the same time, the muscles attached in various complicated ways to the bony cage expand it also, chiefly by an outward and upward rotation of the ribs which, at rest, hang in a rather loop-shaped fashion around its sides (fig. 41 *b*). It is important to remember that on the lower side of the diaphram are the contents of the abdominal cavity (fig. 53). It does not matter for the moment what these are, so long as we realise that the abdomen is quite full, and if its upper boundary is depressed then room has to be made for its contents somewhere else. This is achieved by relaxation of the muscles on the front of the abdomen, a fact which can readily be observed by anyone who takes the trouble to do so.

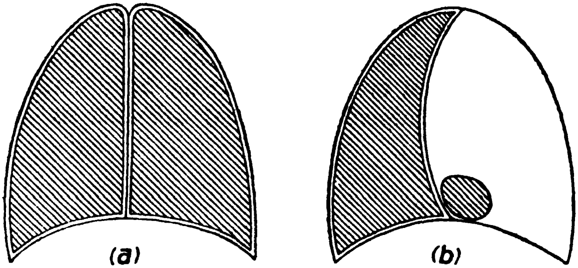

FIG. 71.

(*a*) The normal state of the lung, its outer surface in contact with the inner walls and partitions of the chest . (*b*) The effect of admitting air between the surface of the lung and the inner wall of the chest.

Emptying of the lungs can be brought about by the action of muscles surrounding the chest, which reverse the movement of the ribs, and by simultaneous contraction of the abdominal muscles which force the contents upwards into the dome of the diaphram which is now relaxed. Although the appropriate movements of all these muscles take place during quiet respiration, they are not very forceful. The reason is that the elastic fibres in the lungs themselves are sufficient, when the muscles of inspiration cease contracting, to restore the thorax to its normal shape by simple recoil. It is necessary, however, in the erect posture for the abdominal muscles to take the weight of the abdominal viscera. During breathlessness the muscles of expiration are brought more forcibly into play, and in actual asphyxia their contraction may be so strong and so reinforced by almost every muscle in the body that the act of expiration (or attempted expiration) amounts to a general convulsion.

Artificial respiration

The best known method of artificial respiration (Schafer's) depends on using the weight of the person applying the treatment to make the volume of the thorax even smaller than it normally is in the naturally relaxed position of expiration. When the weight is removed the thorax recoils to the expiratory position and thus produces an inspiration which finishes where a normal inspiration would begin. Details of this method are given in most physiology text books and books on first aid. It is noteworthy that the weight is applied to the back of the subject over and below his lowest ribs. What it really does is to force his abdominal contents further up into the dome of the diaphram. *Eve's method* cannot usually be applied immediately in an emergency, but it is not difficult to improvise the necessary apparatus to which the patient can then be transferred. It consists essentially of a see-saw to which the patient's body is tied and on which he can be slowly rocked with his head and heels alternately in the low position. The abdominal contents alternately press against the diaphram and push it up into the thorax, then fall in the opposite direction and pull it down. This pulling creates an inspiration which bears rather more resemblance to normal inspiration than that produced by Schafer's method. It has the additional advantage of not tiring the manipulator.

Central control of respiratory movement

The chief motor nerve of respiration is the *phrenic* (fig. 72), which supplies the diaphragm. It arises from a motor centre in the upper part of the spinal cord. (There are other motor centres which innervate the other muscles of respiration, and their activity may be regarded as parallel to that of the phrenic nerve.) This centre in the spinal cord is itself incapable of maintaining respiration, for if it is separated by surgical methods from the higher parts of the central nervous system, then it ceases to function and asphyxia follows.

There are two other groups of cells in the medulla which act reciprocally (fig. 72), one which excites the motor centres of the inspiratory muscles (e.g. the diaphragm) and the other which excites the motor centres of expiratory muscles (e.g. the anterior abdominal muscles). These centres act alternately, causing inspiration and expiration, and while one is discharging the other is inhibited. The reader will remember that in speaking of muscular activity we mentioned reciprocal innervation of the

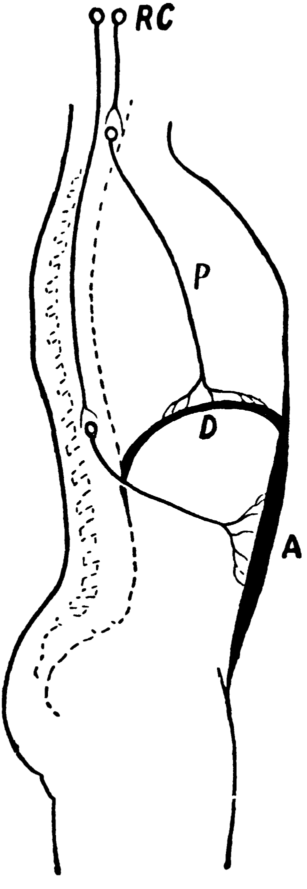

FIG. 72. To illustrate control by the respiratory centre (RC) of the reciprocal activity of the diaphragm (D) and abdominal muscles (A).

P is the phrenic nerve which rises in the neck and traverses the length of the chest to gain the diaphragm.

muscles of the arm. This is much the same kind of thing, but the respiratory centre, taking it as a whole, has the power of *spontaneous* rhythmic activity. That is to say, it will still work when cut off from the higher parts of the nervous system, though its rhythm may not be normal. Normal rhythm is ensured by a third centre in the pons which seems to have a regularising influence. Higher centres still can modify respiration. For instance, we can voluntarily hold our breath or speed up the rhythm for a short time.

This chain of centres merely furnishes what might be termed the skeleton of respiratory control. Respiration is further modified by impulses carried to the centres by afferent nerves. Some of these doubtless come from the respiratory muscles themselves, so that the central nervous system may be kept informed at every instant of the degree of muscular activity which it has evoked. But probably the most important are those carried in the vagus nerves. These collect impulses from the lungs, thereby providing the central nervous system with a record of what is happening to the structures which matter most and which are also the most delicate. During inspiration, that is during stretching of the lungs, showers of impulses pass up the fibres of the vagus nerves, and the mixture of excitation and inhibition thus produced in the brain stem has the effect of damping down the action of the inspiratory centre and enhancing that of the expiratory centre. During expiration, i.e. partial collapse of the lungs, the impulses in the vagus are greatly reduced in number, culminating in the release of the inspiratory centre from inhibition and a lowered excitability of the expiratory centre. Inspiration thereupon takes place. The vagus nerves can be cut in anaesthetised animals and the change caused in the rhythm of respiration is remarkable. Expiration and inspiration continue, but each act is much more prolonged than usual with the result that breathing is deeper and slower. If we sever the connection of the main respiratory centre with the controlling centre in the pons, then other irregularities occur, and it is clear that although the inspiratory and expiratory centres can " carry on " by themselves, they are dependent for *normal* activity upon secondary nervous connections.

Chemical control of respiration

We have already stated that the volume of respiration is greatly influenced by the amount of carbon dioxide in the blood. If carbon dioxide is not removed rapidly enough, hydrogen ion concentration tends to increase, and acts as a powerful stimulus to increased ventilation, which then enables the pressure of carbon dioxide in the depths of the lungs to be reduced. All the nervous framework of respiration which we have described is, in fact, subordinate to the chemical composition of the blood. So far as we can tell this exerts a direct action on the cells composing the respiratory centre by the change which it produces in their immediate environment.

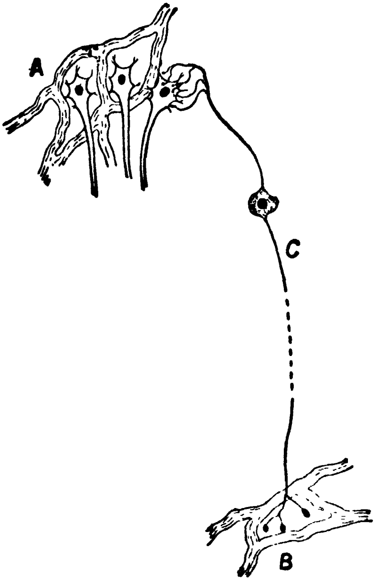

FIG. 73. The Chemical control of respiration.

A, Blood acting directly on cells of the respiratory centre. B, Blood acting on nerve endings in the carotid body. C, The nervous connection between carotid body and respiratory centre.

The direct chemical action on the centre is reinforced by nerve impulses which influence the centre in exactly the same direction and which arise in the *carotid bodies* (fig. 73). These are two minute groups of sensory nerve endings in the large arteries running through the neck to the brain. Like the cells of the respiratory centre, these nerve endings are sensitive to the carbon dioxide content of the blood. Some of them also have the power of responding (by emitting appropriate nerve impulses) to lack of oxygen in the blood. Possibly on account of the exquisite sensitiveness of the carbon dioxide mechanism the " oxygen-lack " mechanism is rather sluggish. Perhaps it does not get enough practice. After all, in normal circumstances the elimination of large quantities of carbon dioxide is coincident with the utilisation of large quantities of oxygen and it is immaterial which of these mechanisms responds. Since the carbon dioxide mechanism has additional interests of its own to serve (regulation of the hydrogen ion concentration of the blood) it can safely be left to do the work for both. In modern life, however, we cheat the body by exposing ourselves in aeroplanes and upon high mountains to conditions in which the carbon dioxide mechanism *cannot* be entrusted with sole control. Under such conditions it blindly looks after its immediate interests, and the body is threatened with oxygen lack until the structures responding specifically to this deficiency assume control. When they do this the working of the carbon dioxide mechanism is upset, and the body has to deal with the ensuing complications as best it can.

Meanwhile, we may conclude that rhythmic movements of the respiratory mechanism are initiated and maintained by a complicated system of nerves and nerve centres, several components of which we can distinguish, and that the activity of the whole can be made to wax and wane by very small changes in the chemical composition of the blood. Normally this chemical control is vested in a " carbon-dioxide-sensitive " mechanism, reinforced to a slight extent by an oxygen-lack mechanism. In certain circumstances the oxygen-lack mechanism takes precedence and, while maintaining life, gives rise to complications.

CHAPTER XIII

EXERCISE, WORK AND ATHLETICS

If we now glance back over the first two or three chapters of this book, it will be apparent that there is something we can add to them. We said that when foods were burnt in an apparatus which allowed their heat production to be measured, the latter was identical with the amount of heat they produced in the body (using heat as the final measure of all energy derived from food). There is another aspect of this statement which we did not explore. If food is burnt outside the body it must use oxygen, and the same weight of the same food will always need the same volume of oxygen. In combustion experiments foods are, in fact, always burnt in pure oxygen so that the amount which has been used can be measured. In this way, we find that:

1 gram of sugar or starch yields about 4 kgm.-cals. of heat, consumes about 800 cc. of oxygen and produces about 800 cc. of carbon dioxide.

1 gram of fat yields about 9.5 kgm.-cals. of heat, consumes about 2000 cc. of oxygen and produces about 1400 cc. of carbon dioxide.

1 gram of protein yields about 4[1] kgm.-cals of heat, consumes about 960 cc. of oxygen and produces about 770 cc. of carbon dioxide.

Practically everything we eat can be classified under one or more of these three headings. For instance, bread is predominantly carbohydrate in nature, butter is pure fat, and lean meat or fish contains little besides protein. (Vitamins and salts have no useful energy value in themselves.) The figures we have given show that *for each class of foodstuff there will be a certain number of kgm.-cals. of heat produced for each cc. of*

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[1] Burnt outside the body, protein produces rather more heat than this, but in the body some of its nitrogenous breakdown products are not completely disintegrated and some of its potential energy is, therefore, wasted. As our interest lies in what goes on in the body we have used the lower figure in the text.

oxygen breathed. It happens that foods differ very little in this respect, as the reader will readily confirm by doing a little arithmetic. 1 litre of oxygen yields about 5 kgm.-cals. of heat whatever foodstuff is utilised. This simple fact opens up great possibilities. It means that we do not need to put people in a calorimeter (fig. 5) to find out how much heat they are producing per hour or per day: we need only measure their oxygen consumption.

If we happen to be interested rather in finding out the kind of food a person is oxidising at any moment than in his energy production, we can make use of the figures in another way. Since protein alone of the foodstuffs contains nitrogen and since all nitrogen is eliminated in the urine, we can collect the urine over a given period, measure the amount of nitrogen it contains and calculate the amount of protein which this represents. This is the weight of protein utilised during the period in question. It corresponds to the consumption of a certain volume of oxygen and the production of a certain volume of carbon dioxide. These volumes can respectively be subtracted from the total utilisation and production during the period of the experiment. Now the rest of the oxygen and carbon dioxide must represent the combustion of some mixture of fat and carbohydrate because these are the only two remaining classes of foodstuff. It will be observed from the information given above that, whereas the ratio of carbon dioxide production to oxygen consumption is 1 for carbohydrate, it is only 0.7 for fat. All we have to do, therefore, is to work out the ratio of carbon dioxide to oxygen in the actual experiment and a little further calculation enables us to say what *proportion* of carbohydrate and fat it represents. Since we know the oxygen consumption has a definite volume, we can learn not only the proportions of these two foodstuffs used, but their actual weights. We now know the actual weights of protein, carbohydrate and fat consumed over a certain period of time. If we wish to know accurately the rate of energy production, we can use these weights to derive the calorie equivalent of each foodstuff instead of using the over-all approximation of 5 kgm.-cal. per litre of oxygen consumed.

There are many ways of measuring oxygen consumption. One of the methods, shown in fig. 74, consists in allowing the subject of the experiment to breathe from a gasholder, and measuring the distance through which the bell of the gasometer falls. In order to eliminate the return of carbon dioxide to the

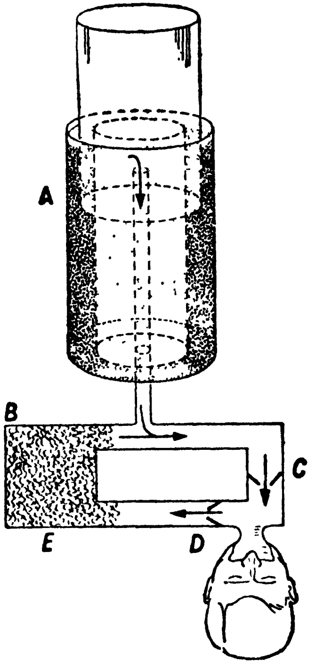


FIG. 74. The measurement of oxygen consumption.

A. Oxygen container. B. Main respiratory circuit with valves at C and D, and a carbon dioxide absorbent at E. The volume of each expiration is reduced as it passes through E, so that when the subject inspires to the same degree, part of the oxygen in A is drawn into the respiratory circuit, and the bell of the gasholder falls. (The suspension of the bell, the recording of its movement, and the clip on the subject's nose, are not shown.)

gasometer this gas is absorbed by alkalies. A disaster such as we mention on page 141 arising out of the using up of oxygen is obviated by filling the gasometer with pure oxygen or with air to which a large quantity of oxygen has been added. Since this method requires a special circuit of tubes and bottles and a gasholder it can only be used for a subject at rest or doing some exercise in a stationary position. It is much used in medical work for measuring the basal metabolic rate. But for finding out oxygen consumption during different kinds of activity in normal persons, a much more adaptable method, introduced by the English physiologist, Douglas, is used.

The subject's nose is clipped and the mouthpiece of a valve inserted into his mouth through which he breathes inwards from the atmosphere and outwards into a rubber-lined bag, which he carries on his back and which is connected to the mouthpiece by a wide flexible tube (fig. 75). The bag is big enough to contain about 60 litres of " expired air ", and it is left in position until it is almost full. Quite a small sample—say 25 to 50 cc.—is

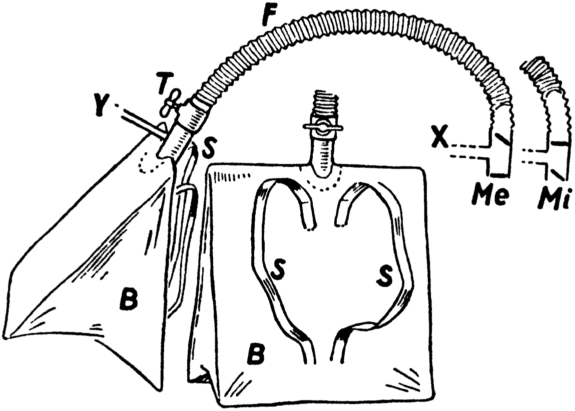


FIG. 75. Portable apparatus for measuring oxygen consumption.
B, bag attached to subject by strap S, and connecting with subject's mouth by means of the flexible tube F and a mouthpiece X. When the subject inspires and expires the valves of the mouthpiece are in the positions shown in Mi and Me respectively. T is a tap to close the bag after use and Y a fine side tube for removing samples. When not in use it is clipped.

removed and analysed so as to indicate the composition of the air in the bag. It may be 4 per cent carbon dioxide, 16 per cent oxygen and 80 per cent nitrogen. The remaining air in the bag is then squeezed out through a gas meter which accurately measures its total volume. Since we know what percentage of the total is oxygen, we can calculate the actual volume of this gas which has been breathed out in the measured time. If we knew what volume of atmospheric air had been breathed in during that time and the percentage of oxygen which it contained, we could similarly obtain the volume of oxygen breathed in. The difference between this and the volume in the bag would be the amount used by the subject. Now the *composition* of atmospheric air is practically invariable, and it is safe to assume that it contains 20.93 per cent of oxygen, 0.03 per cent of carbon dioxide and 79.04 per cent of nitrogen and other inert gases. If there is any doubt about it, it can be analysed on the spot. The *volume* breathed in can be worked out in an ingenious way from the composition of the expired air because *the lungs neither add nor subtract nitrogen from the air* The quantity of nitrogen in the bag, therefore, is exactly the same as the quantity of nitrogen breathed in during the experiment, and every 79.04 cc. represents an intake of 20.93 cc. of oxygen. In short, the actual procedure necessary to determine the rate of oxygen consumption of a person consists in collecting his expired air for a carefully timed period, analysing a sample of it and measuring its total volume. The rest is arithmetic.

This simple procedure enables us to obtain figures for oxygen usage under a variety of conditions and the chart in fig. 76A shows the astonishing flexibility of the body as a machine. It will be seen that oxygen intake can vary between about 250 cc. a minute under resting conditions to 6 litres per minute during very strenuous exercise. We will discuss the chart and its implications. The first five records are self-explanatory and mean that the more work we do, the more oxygen we consume.

The last three, however, require some comment.

The last record is of an Olympic games boat crew, and over a period of *22 minutes* the oxygen intake of its members ranged between 4 and 6 litres per minute. Although this represents a maximum effort, so does the preceeding level on the chart of about 2 litres per minute, the difference being that the latter was maintained for *several hours* by experts in pursuits like bicycle riding, long distance running, mountain climbing and swimming. The figures furnish striking confirmation of the universal experience that the harder is the work, the shorter is the time during which it can be sustained. Level No. 6 represents the oxygen consumption of a man walking at 5½ miles per hour, which is somewhat more than an athlete can maintain for 4 or 5 hours. The best way, therefore, of gaining an idea of the degree of work which can be kept up for a long period is to try walking at this speed.

When we are dealing with bursts of exercise maintained for less than half an hour, the phenomenon mentioned on page 93 becomes important. This is the ability of muscles to contract for a time without oxygen, and to take up the oxygen later. An athlete does not always breathe during a 100 yard race, and certainly need not do so in a 60 yard sprint. The amount of

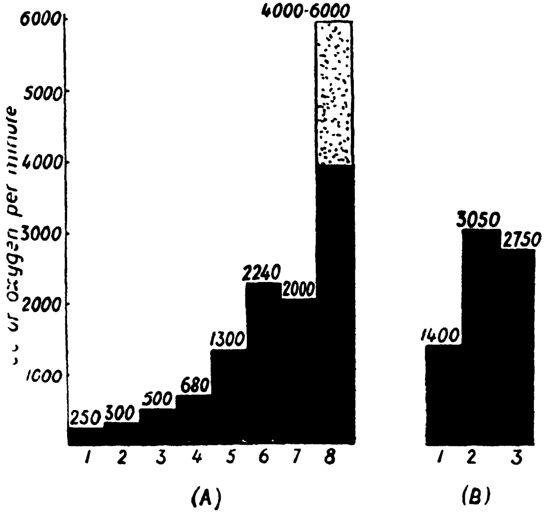


FIG. 76. A. Levels of oxygen consumption under various conditions of rest and exercise. Rate of consumption is indicated in c.c. per minute at each level.

(1) At rest lying. (3) Swinging arms. (5) Walking at 4.2 m.p.h.
(2) At rest standing. (4) Walking at 2 m.p.h. (6) Walking at 5.4 m.p.h.
(7) Championship cycling, running, climbing or swimming sustained for three or four hours.
(8) Olympic games events sustained not longer than 20 minutes.

B. Total oxygen consumption when running upstairs 12.2 metres high.

(1) In 100 sec. (2) In 24 sec. (3) In 250 sec.
The very fast and very slow performances are wasteful of energy. *Rate* of oxygen consumption is very different in the two cases, being extremely high in the former and low in the latter.

oxygen which corresponds to the muscular effort involved is breathed in afterwards, can then be measured, and is appropriately called *the oxygen debt.* If during a 100 yard sprint lasting 10 seconds an athlete does not breathe, but afterwards takes in 4 litres of oxygen over and above his normal consumption we can say that although he actually used no oxygen while running, he was working at a rate *equivalent* to an oxygen intake of 24 litres per minute. Even higher rates of work than this have been found, and it is thought that the limit to the rate of work for periods short enough to be covered by an oxygen debt is not chemical, but is dictated by mechanical factors, such as the breaking stress of the bones and the internal resistance of the muscles to deformation.

If the exercise is of longer duration, it becomes dependent on a *continuous* supply of oxygen, and cannot proceed at a rate much greater than 4 litres per minute (level 8, fig. 76). Even this cannot be maintained for more than a few minutes, and when we consider really long bouts of exercise we find that 1.5 to 2 litres per minute is the maximum intake which can be sustained. At 4 litres per minute a limited reserve of some kind is being freely drawn upon, but even 1.5 litres per minute cannot be kept up for more than a few hours. This can be appreciated by thinking of it in terms of calories. If the use of 1 litre of oxygen represents the expenditure of 5 kgm.-cals. (p. 158) then work is being done at 7½ kgm.-cals. per minute or 450 kgm.-cals. per hour. In 6 hours, a person working at this rate would use 2700 kgm.-cals.—nearly as much as the average man uses in 24 hours.

Returning for a moment to the question of oxygen debt, we find that it can be used to " boost up " the energy available for brief muscular efforts. The biggest total oxygen debt which has been recorded is about 19 litres, and a figure of 15 litres is conventionally assumed for a man in training. If he can supply oxygen to his muscles at 4 litres per minute, and go into debt to a total of 15 litres, then for 15 minutes he can work *at the rate of* 5 litres per minute. If, however, he miscalculates and runs at a speed requiring 7 litres of oxygen per minute, he goes into debt for 3 litres every minute, and he will be able to keep up his effort for only 5 minutes.

That there should be a limit to the oxygen debt is easy to understand—it is an expression of the point at which muscles have no reserve of energy unless they begin to oxidise carbohydrate, or at which they become affected chemically by waste products. The two things, as it happens, are closely related. Before the glucose which comes from glycogen is finally oxidised, it may itself split up to form a new substance, *lactic acid*. It will certainly do so if oxygen is withheld, but when oxygen is readmitted the lactic acid is oxidised as though no hitch had occurred. This substance not only represents fuel waiting for final combustion in a muscle which has gone into oxygen debt, but is also capable of poisoning the muscle if it reaches a sufficient concentration (0.28 per cent). The reader has probably (and most commendably) thought that the accumulation of lactic acid may set the limit to the rate at which work of a few seconds duration can be performed, rather than the somewhat vague mechanical factors we have mentioned. This is not so, however.

We have seen that the rate of work in a sprint may *correspond* to 25 litres per minute oxygen usage. A chemical investigation of the combustion of lactic acid outside the body shows that this rate is equivalent to the accumulation of about 3 gm. of lactic acid per second, or a total accumulation of 30 gm. in 10 seconds. The question is whether 30 gm. represents a poisonous concentration. The answer is no. Even if none leaked into the blood and general extra-cellular fluid, 30 gm. in 35 kgm. (the approximate weight of the musculature) is less than 0.1 per cent. If only half the musculature is regarded as active, with still no leak into the blood (both extreme assumptions), we get less than 0.2 per cent, and it is obvious that 0.28 per cent is not achieved, and accumulation of lactic acid is therefore not a limiting factor in such brief spurts of exercise.

There are two things which we still have to explain. First, why it is that during a heavy burst of work the body can take in only 4 litres of oxygen per minute, and secondly why, if the work is prolonged, the intake of oxygen can be maintained at only about 1½ litres per minute.

The best way to discover limiting factors is to follow the track of oxygen from the air to the cells and look for the likely places where the transport may become insufficient. First of all there is the pressure of oxygen in the alveolar air. This has never been known to drop below 100 mm. of mercury in normal individuals even during severe exercise, and there is no evidence whatever that the actual mechanical processes of filling and emptying the lungs ever fail to keep pace with the requirements of the body for oxygen.

The first obstacle which the oxygen encounters is made up of the cells of the lung alveoli, of the capillaries, and of the fluid which may lie between them. Does this obstacle ever hinder the passage of oxygen? In more concrete terms, when the blood is flowing fast through the lungs and the rate of transfer of oxygen is high, does the blood ever leave the lungs incompletely saturated with oxygen in spite of a normal pressure being maintained in the alveoli? It must be admitted that this is a possibility, and, in fact, slight degrees of unsaturation of the arterial blood have been observed. (In persons suffering from illness, particularly if this involves the lungs, the head of 100 mm. of mercury pressure may be definitely insufficient to drive oxygen quickly enough through a water-logged or a thickened alveolar membrane). It seems, however, that we must look further, because if the arterial blood were seriously unsaturated the obvious signs of distress would be accompanied by a blueness of the lips and face, and this does not happen in health.

Closely related to the anatomical factors which determine the rate at which oxygen passes from alveolar air to blood are the factors at the other end of the circulation which determine the passage from blood to cells. It has been found that, when a muscle is at rest, a great many of the capillary blood channels through it are closed and the circulation trickles through only a restricted number. One of these capillaries can be pictured as responsible for the supply of oxygen (and other material) to the cylindrical block of tissue which surrounds it, and we may assume that the cells on the outer fringe of this " cylinder " are not too far away to get their oxygen fast enough. The factors on which the transfer depends are similar to those discussed on p. 148. Should the muscle be thrown into activity these remote cells would suffer from oxygen lack if it were not for the fact that thousands of other capillaries in the muscle open up and the blocks of tissue for which each capillary is responsible are greatly reduced in size. It is believed that this increase in the capillary bed of muscle, which is now very liberally irrigated with blood, neutralises to a very large extent the physical obstacles to oxygen uptake.

It is almost certain, however, that in spite of this a certain minimum pressure of oxygen must be maintained in the blood in order that oxygen shall pass rapidly enough to the cells, and this critical pressure is about 20 mm. mercury (corresponding to an oxygen saturation of about 30 per cent). At first sight it seems surprising that the blood should have to leave the tissues with almost a third of its original load of oxygen. But we do not know the precise condition under which the *cells* work. It is unlikely that they can function adequately if their own oxygen pressure is zero. Perhaps if it falls below 20 mm. mercury in the blood an essential chemical process may have to slow down or stop. Perhaps the " fluid barrier " between haemoglobin and cells is so much thicker than the corresponding barrier in the lungs that the oxygen pressure on the " blood side " must be kept fairly high to push the molecules of oxygen through quickly enough to the " cell side " to replace those removed for oxidative processes. If there is any resistance of this kind to molecular movement, the speed of movement always depends on the " pressure gradient " across the resistance.

The graph in fig. 77 shows that a trained athlete is able to keep

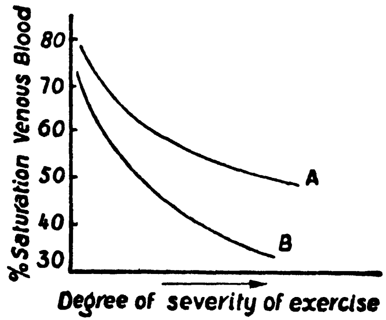


FIG. 77. To show how the blood returning to the heart becomes more and more depleted of oxygen as exercise grows more severe. The curve A refers to an athlete in training Curve B to a person out of training (after Bock *et al.*, *J. Physiol.* Vol. 66).

a reserve of oxygen in the blood leaving his muscle during exercise, whereas a person out of condition fails to do so. On the other hand, the *resting* individual uses only about one-third of the oxygen presented by the blood to his muscles. Our conclusion is that the muscles may benefit by making *more* use of the oxygen in the blood, but they cannot use *all* of it because some condition for utilisation imposes a limit below which the oxygen pressure in the blood must not fall.

However, if blood is brought to the muscle in sufficient quantity, it can supply oxygen to the muscles and still maintain a reserve as it leaves, and this brings us to a new set of considerations altogether, involving those factors which determine the volume-flow of blood through the tissues. Limits to the rate of transfer from blood to cells come into play only if the limit of blood supply has been reached, and the blood seriously depleted of oxygen. There is no evidence that blood ever passes through muscles *too quickly* for oxygen to be removed from it. So long as its oxygen pressure does not fall too low, the cells can seize the oxygen in time. They are probably helped in this by the fact that the protoplasm of the muscle cells contains a kind of haemoglobin.

We have very largely covered questions of supply in Chapter VIII. It is evident that the opening up of closed capillaries in muscle, and the further dilatation of arterioles and capillaries already patent, has two main consequences if work is being done by the muscles. (1) The flow of blood through other parts of the vascular system must be curtailed and their capacity diminished and (2) the blood must be circulated so rapidly that the supply per minute to the muscles is increased to a degree commensurate with their additional capacity and with the increased oxygen utilisation of the individual fibres. The natural consequence of increased capacity would otherwise be a slowing of the stream, in much the same way as the speed of a river diminishes when the bed widens considerably. It is no use having that quantity of blood per minute which was sufficient during rest simply distributed more thoroughly in the active muscle. The blood flow must be sufficiently rapid that the individual member of a chain of corpuscles passing through a blood channel does not stay long enough to be depleted of more than about two-thirds of its oxygen. The muscle is not deprived of the remaining one-third, but gets it from the succeeding corpuscles in the train which should follow along fast enough to keep up the supply, and, at the same time, maintain a sufficient oxygen pressure in accordance with the principles we have just discussed.

The important demand is, of course, due to the chemical activity of the muscles, and a comparison of the oxygen utilisation of exercise with that of rest is a sufficient indication of the increased requirement for oxygen. The demand, over and above that which is met by plain redistribution, falls directly on the heart, which is the main pumping mechanism. The muscles themselves possibly act as auxilliary pumps because they are alternately contracting and relaxing, and as there are valves in the veins which allow the blood to flow in only one direction, the return of blood to the heart may be assisted. It is arguable, however, that while a muscular contraction helps blood out, it is, at the same time, obstructing blood flowing in, so that it is not really helping the heart, but merely refraining from hindering it. The ability of the heart to pump blood round the circulation sufficiently fast is, therefore, regarded as the limiting factor to all forms of exercise which last for more than a matter of seconds or minutes, i.e. which depend for their maintenance on the oxygen supply from moment to moment.

The heart itself is a muscle and the only rest it gets is between beats. The exact nature of fatigue is unknown, but it is safe to say that it is due to the exhaustion of some factor which is made good by rest. If the heart has insufficient rest between beats, as is probably the case with an athlete doing exercises which will exhaust him in the course of fifteen to twenty minutes, then it will protect itself after a time by increasing the interval between beats and will finally have to be allowed to beat at a fairly slow rate in order to recuperate. Exhausting exercises too frequently repeated may have a deleterious effect on the heart. Similar considerations apply to exercise which can be carried out for three or four hours. The difference is that the proportion of rest to work which the heart gets during the exercise is higher.

There is only one thing more to be added to our account of the principles involved. We are not correct in assuming that the increased rate of blood flow is due altogether to an increased *frequency* of the heart beat. It has been established that as the demand increases, the *volume of blood pumped out by each beat* of the heart is increased. Some persons achieve a greater cardiac output chiefly by means of increased rate, others chiefly by means of increased stroke-volume, but when they are completely extended both potentialities are exploited to the full.

Optimum Rate

In the second chart in fig. 76 are shown three levels which depict not rates of oxygen consumption but total oxygen consumption. The work done in each of the three cases was identical. The subject ascended the same flight of steps three times. When he went up quickly (in 24 secs.) and when he went up very slowly (in 250 secs.) his oxygen consumption was high, but when he went up at a medium rate (in 100 secs.) his oxygen consumption was practically halved. We can state our conclusion quite briefly if we recall our definition of a machine. The man is inefficient going upstairs quickly or going upstairs slowly, but somewhere between the two extremes there is a rate of ascent which gives the greatest efficiency. There are many ways of showing this and it is important in everyday life. One part of the attainment of skill, in any pastime or professional activity which involves muscular co-ordination, must be the performance of the necessary movements at the best rate. The mechanics of muscular contraction and the experiments on isolated muscle which elucidate this point in terms of the properties of muscle make a fascinating chapter of physiology, which is rather too technical for us to tackle in this book.

Integration

The word " integration " has been given a rather special meaning by physiologists, and the way in which additional oxygen is supplied to an active tissue furnishes a good example of it. It means that when the body can achieve a certain result in more than one way it tends to make use to a moderate degree of all the possibilities open to it, in preference to exploiting one mechanism to the full, then reinforcing it by a second, and then by a third and so on. For instance, if the output of the heart is to be increased, the increase is not brought about by the heart first accelerating until it can go no faster and then beginning to increase its stroke. Both the frequency and the stroke volume are increased simultaneously, though not necessarily equally. At the same time, the tissues take more of the oxygen which is presented to them, so that the blood leaving the muscles carries a smaller load of oxygen back to the lungs and can, therefore, accept more as it traverses the pulmonary circulation.

Another adjustment which we touched upon in Chapter VIII is a contraction of the spleen. This somewhat spongy organ contains a certain amount of blood which comprises an unusually large number of red cells. When these are squeezed out, each cubic centimetre of blood in the circulation contains rather more red cells than it did before, and can therefore carry a little more oxygen. There are indications that red cells may enter the circulation from other storage places as well. This probably represents a relatively minor but yet significant contribution, and calls to mind a " long-term " adaptation of some interest. A greatly increased circulation rate involves wear and tear of the blood cells, and in a person unaccustomed to exercise a severe bout of physical work may lead to a sufficient destruction of the cells to render a second performance much less effective. In trained athletes it is found that this destruction is immediately made good, and that the red bone marrow, which is the place where the cells are manufactured, occupies a much greater proportion of the cavity of the bones than it does in sedentary individuals. It is possible that this also helps athletes to make a more effective immediate readjustment in the way of increasing the haemoglobin concentration of the blood during the exercise itself.

The beneficial effects of integration can readily be seen when we give numerical values to the various adjustments. Suppose that for a given exercise the heart rate is doubled, the output per beat increased 1½ times, the utilisation of available oxygen in the blood doubled and the concentration of haemoglobin increased by 10 per cent, then we have an increased delivery per minute of oxygen of $2 \times 1\frac{1}{2} \times 2 \times 1\frac{1}{10} = 6.6$ times the resting delivery. None of the adjustments by itself could have produced this increase, which is a fairly large one, but even with smaller increases the same principle applies. If its nature is properly grasped the reader will see that we have met it before. The opening up of blood vessels in the working muscles, the redistribution of blood in the body, the increase in frequency and depth of respiration and a host of other adaptations all show that the final result is dependent on the integration of numerous factors so that they work harmoniously to the same end. Much of the integration is carried out by the central nervous system.

CHAPTER XIV

THE SOURCE, FUNCTIONS AND SUPPLY OF FOOD

RECENT years have seen a wide dissemination of knowledge about food and diet, and nearly all who read this book have had practical experience of the restrictions which can be made in a normal diet without producing ill-effects. In referring to food as fuel we have been able to take for granted that we were not going altogether outside of common experience. It is now necessary for us to enquire a little more closely into the nature of food and the way in which it is made available to us.

The material we eat and drink has three main functions. First of all it supplies fuel for work and warmth. Secondly, it replaces the actual material of which the body is made; this is usually referred to as repairing wear and tear. Thirdly, it supplies substances in whose absence certain chemical reactions in the cells fail to occur, or occur in a modified form.

If we take a very broad view we can detect a similarity between the second and third functions. The " stuff " of which cells are made cannot be regarded in the same way as wood and bricks and concrete and other materials of which inanimate objects are made, because it is all the time so very active. It is more correct to regard it as a conglomeration of substances which are perpetually reacting chemically in order to divert energy to their own particular purposes. Thus, when we say that cells are suffering from wear and tear, we may really mean that one of the substances which they contain is becoming used up; but we know too little about the precise way in which the cell works to put our finger on the deficiency. In the case of simple substances such as salts and traces of various metals, we can sometimes be definite, and when, for instance, the formation of red blood cells breaks down because there is insufficient iron in the diet, we speak of " a deficiency in iron " rather than of " wear and tear of the bone marrow " which is the place where red cells are made. Many quite complicated substances usually called *vitamins* are now known to be essential to the proper functioning of cells, and since we are aware of their nature we refer again in precise terms to a deficiency of one or other of them.

We shall adhere to the usual custom of referring to " wear and tear " and " deficiencies " as though they were different, but we must bear in mind that the ordinary foodstuffs as well as minerals and vitamins contribute to the upkeep of chemical processes as well as to mere structure.

It is often taken for granted that protoplasm is synonymous with protein, and that the latter foodstuff, which is found in high concentration in the cells of animals (e.g. meat and fish) is their only constituent. Protein, therefore, is usually looked upon as the chief source of material for repairing wear and tear. There is just sufficient truth in this idea to make it too easily acceptable. The actual facts of the case are that fat is also an integral part of the protoplasm of cells, though it may be present in a combined form and therefore not visible even microscopically as globules. When it is visible, this means that it is not part of the protoplasm of the cell at all, but is simply being stored by the cell until it is needed. The same is true of carbohydrate. Nervous tissue, for instance, is very rich in substances containing carbohydrate and fat in combination, while the nuclei of all cells contain a substance called nucleic acid which is part of the protein special to nuclei and which itself contains combined carbohydrate. All three of the main classes of foodstuffs—proteins, fats and carbohydrates—furnish not only fuel but the actual substances which form the basis for the activities of protoplasm.

The importance of protein for the maintenance of cells lies in the fact that it is the only source of nitrogen which the animal body can use to manufacture its own protein. Fat and carbohydrate cannot supply nitrogen. Therefore, in the absence of protein in the diet, wear and tear cannot be made good. On the other hand, wear and tear can be made good in the absence of fat and carbohydrate, because proteins do contain the elements necessary for building up these substances. Fat can also be made from the elements supplied by carbohydrate, and it is possible that carbohydrates may be made from fat. In our ordinary diet, carbohydrate and fat exist in such quantities that we regard them as our chief sources of energy, but this does not mean that they have no other function.

The nature of food

The chemistry of the foodstuffs is a specialised study into which we do not need to enter in detail. In various places we have already said practically all we need on the subect. We can add a few points and say a few words about their significance.

Proteins have very large molecules which contain nitrogen, and they form a high proportion of the constituents of protoplasm. Most meats and fish contain from 12 to 15 per cent of protein out of a total of about 20 per cent of solid material, the rest being water. The best example of a solution of practically pure protein is the white of egg. The constitution of the protein molecule is fortunately not difficult to understand. It is made up of hundreds of smaller molecules called *amino-acids* which have been joined together in such a way that it is possible for chemists to split them off singly or in groups and find out which they are. About twenty animo-acids are known, and as their name suggests, they are built on a common plan, and all contain nitrogen. The differences between proteins depend on the number of amino-acids which are linked together to form them, on the particular method of linkage, and on their spatial arrangements within the molecule. The protein of voluntary muscle is different from that of smooth muscle. Both are different from the proteins of the blood plasma and of egg white, and so forth.

These differences are important in relation to the functions which proteins perform in the body, but not so important when we are merely regarding them as food. In this respect they may be looked upon as collections of amino-acids, because this is the form in which they are assimilated.

There is one important qualification to this statement, namely, that some proteins, particularly those found in vegetable cells, are deficient in certain amino-acids essential to the animal body. It is possible for a person to have an apparently sufficient weight of protein in his diet, but to suffer nevertheless from lack of material which only protein can supply. Certain amino-acids are, therefore, called " essential ". They belong to that class of substances, like iron and vitamins, which the animal cannot manufacture for himself and whose deficiency is known to produce certain definite effects. " First class protein " contains all the essential amino-acids; " second class protein " is valuable as a source of amino-acids in general, but does not supply a complete range.

An important feature of the chemical constitution of proteins is their content of nitrogen and other elements such as phosphorus and sulphur. Not only do they represent an important source of such elements—a source of critical importance so far as nitrogen is concerned—but the unused portion of the elements presents a problem to the body to which we have hitherto referred only in passing. They cannot be got rid of by oxidation. This accounts for the fact that a protein does not have quite the heat-producing value when burnt in the body that it has when it is more completely burnt outside the body. The problem of the disposal of non-oxidative waste is not solely associated with proteins. The diet contains many mineral substances which are not used even partly as fuel and which are taken in excess of the body requirements. They, and the unoxidised remnants of proteins, are excreted in solution in the urine which will be dealt with in Chapter XVII.

Fat. Chemically speaking fat is much simpler in construction than protein. In its most common form it consists of three molecules of substances known as fatty acids, linked together by the comparatively small molecule of glycerol. The fatty acids are the really important part of this type of compound, but their combination with glycerol confers upon them the peculiar properties we habitually associate with fats and oils. The most familiar edible fats are butter, obtained from milk, and substances like suet and lard, obtained directly from animal tissues. These foods are practically pure fat. They contain very little water or other material. In this they differ from protein foods, which rarely contain more than about 15 per cent of actual protein. Food includes other fat-like bodies in which one or more of the ordinary straightforward fatty acids is replaced by some much more complicated substance which may contain nitrogen or phosphorus or both, and may perhaps incorporate a molecule of carbohydrate. So far as we know these substances, although they occur in various special situations like the brain and bile, need not be assimilated as such. They can be manufactured by the body from materials contributed by the ordinary fats, proteins and carbohydrates.

The only way in which fats are essential is an indirect way. Certain of the vitamins, in particular A and D, are soluble in fats and oils but not in water. If, therefore, there is no fat in the diet, the latter will be lacking in vitamins unless these are administered separately. Vegetable fats, like margarine, do not normally contain either A or D, so we may go a stage further and say that these will be missing if the diet does not contain animal fat. Their most usual source is butter and it is well known that the vegetable substitutes now have the vitamins added to them. Excluding ordinary dietary fats, the usual source of vitamins A and D is fish liver oil. This is just as much a fat as mutton fat or beef fat, but being composed of different fatty acids, the final compound molecule is fluid instead of solid. Solid fat melts if it is warmed sufficiently, however, and in warm-blooded animals the fat may be fluid or nearly fluid during life because it is at body temperature. Except for the rather complex fat-like substances we have referred to, fats contain no elements besides carbon, hydrogen and oxygen, and when they are completely burned, the waste products formed are simply the oxides of carbon and hydrogen, namely, carbon dioxide and water. In some conditions, where the oxidative processes of the body are abnormal (for instance, in diabetes) complete combustion of fats does not occur and certain chemical compounds, often acid in nature, are formed from the fragments of the fatty acid molecule and have ill-effects on the body. From what we said on page 138 about hydrogen ion concentration, it will easily be seen how serious can be the liberation of acid substances into the blood-stream.

Carbohydrates for most practical purposes mean starch, cane sugar and milk sugar until they are taken into the body. There we meet chiefly with glucose and glycogen. Before explaining briefly these terms, and the transformation of one kind of carbohydrate into another, we ought to know that the description " carbohydrate " applies to a great many things we do not ordinarily associate with nutritive food. Much of the supporting structure of plants is composed of the carbohydrate cellulose. This is not used as fuel by human beings, but it is by no means absent from the diet. The skins of fruit, the stalks of vegetables, etc., pass right through the gut from one end to the other and give it a certain amount of " body " or " roughage " to work upon. Fortunately, grazing animals *can* utilise cellulose truly as food, breaking it down into its simple sugary constituents, and from these and the amino-acids of their fodder they can not only supply themselves with energy, but lay down fat and build muscle whose protein includes the " essential amino-acids ". These attainments of animals, of utilising material we cannot, and of making out of it things we cannot, is very important for the human race, which eats the animals or their products.

Carbohydrates resemble fatty acids in containing only carbon, hydrogen and oxygen in their molecules, but these elements are arranged in a different way and are present in a different proportion, and the two classes of substances have quite different properties. Carbohydrates with large complicated molecules, like starch and glycogen, are found to be made up of hundreds of smaller molecules of glucose, which is a relatively simple substance. Thus, although starch and glycogen are suitable, because of their condensed form, for storage, glucose is more useful as currency because of the smaller size of its molecule. Just as the body breaks down protein into its amino-acids before starting to make use of it, so it breaks down starch to glucose.

If the positions of certain parts of the glucose molecule are transposed, a large number of sugars with slightly different properties can be made in the laboratory. Some of these occur in nature, and two are met with in food. These are *fructose* and *galactose*, but they do not often appear, as it were, in their own right. We find them combined each with a molecule of glucose.

The combination of glucose and fructose is very familiar to us as cane sugar (or *sucrose*), and that of glucose and galactose is somewhat less familiar as milk sugar (or *lactose*). Cane sugar is the sweetest of all these substances. It is a relatively simple task for the body to split the molecules of cane sugar and lactose into their respective components, but it makes a really good job of it by adjusting the molecules of galactose and fructose so that they are both turned into glucose. Thus the final product it has to deal with is always glucose. This is readily oxidised, and the cells of the body are continually using it. They do not rely on the load of it which is thrown into the body at each meal, but build up a store of *glycogen* which can be steadily drawn upon between meals, and restored as opportunity offers. The muscles and the liver are the places where most of the store is kept. Glycogen is only different from starch in the way in which the molecules of glucose are arranged within its larger molecule.

Minerals are very simple substances compared with those we have been considering. Although it has little to do with their function in man, it is interesting to reflect that they form one of the principal foods of plants, on which we are dependent directly, or indirectly through other animals which eat them, for our food. The food of plants is the small fraction of carbon dioxide in the atmosphere together with the water and minerals which they extract from the earth.

Mineral substances are not used by the body to furnish energy, but they have a host of important functions which it is impossible to enumerate. We can, however, mention a few examples. *Iron* is built into the protein haemoglobin, so important in the carriage of oxygen, and is also an indispensible factor in the process of oxidation in the cells. *Calcium*, a metal which can be obtained from lime and chalk, is a constituent of bone and so is *phosphorus*. In fact, a well-known mineral, *apatite*, which is a complex of chalk and phosphate, bears a very close resemblance to the substance which gives the hardness to bone. Calcium, like iron, plays an important part in some of the chemical reactions of the body; for instance, blood will not clot unless it is present. Phosphates too are important in another sphere, helping to keep steady the hydrogen ion concentration of the blood and tissue fluid. The body tries to retain minerals of this kind, and only small quantities are necessary in the food. But most of us know that anaemia results from lack of iron, and that deficiency of calcium or phosphate during the years of growth can have deplorable effects on the development of the skeleton.

The salt which we take with our food represents another kind of function which mineral substances have. Each litre of water in the blood and tissue fluid contains nearly 1 gm. of common salt in solution. Just as the processes of life demand a constant concentration of hydrogen ions, so they demand a constant *total* concentration of all the substances in solution in the body fluids. This is not because of what the various ions or substances may do if they are *individually* present in smaller or larger quantities than usual, but because of the consequences of having a generally " too strong " or " too weak " solution bathing the cells. The concentration of many individual components does matter in this respect, but none of them is present in nearly such quantity as ordinary salt. The supply of both salt and water is normally adequate in the diet, and the total concentration of the body fluids is kept constant by the kidneys, which excrete more or less of the surplus of either as occasion demands.

The *intra-cellular water* in man, which is the vehicle in which the constituents of protoplasm do their work, holds substances in solution in the same total concentration as exists in the tissue fluid; but as we have found previously (p. 103) the interchange of soluble material between intra-cellular and extra-cellular water is greatly restricted by the nature of the cell membrane. Salt, for instance, cannot pass across it, and within the cell we find potassium phosphate taking its place (salt is sodium chloride); sodium ions are kept on one side of the membrane, potassium ions on the other.

Let us suppose that, as a result of activity, some of the larger molecules of substances within a cell become broken down into smaller ones. This has the effect of making the solution in the cell " stronger ", even though the total *weight* of solid material dissolved is no greater than before. Space forbids us to explain this apparent contradiction, but there is nothing really mysterious about it; we are using the words " strong " and " weak " to refer to the number and not the weight of units of material in solution, because this is the type of " total concentration " which matters to life processes of the cell. When the solution in the cell becomes stronger, water flows into it from the adjacent tissue fluid until the concentrations inside and outside the cell are the same. If this has happened in a large number of cells simultaneously, both tissue fluid and intra-cellular fluid will be more concentrated, but the latter will be less concentrated than it was just before the exchange. The tissue fluid may be diluted by the drinking of water or the excretion of salt, either of which will make it once more weaker than the intra-cellular fluid. After further adustment between the intra- and extra-cellular fluid, the process will repeat itself on a smaller scale and continue to do so until the original concentration of the intra-cellular fluid has been brought to normal and the strength of the tissue fluid is equal to it.

Vitamins. We have seen that Vitamins A and D occur in fats of animal origin. Both are chemical substances with large molecules and are particularly important for children. It is a matter of common experience that very few nights in the year are so dark that one is unable after a time to see. Absence of vitamin A in the diet is known to give rise to " night-blindness " or inability to see in very dim light, though it is not the only cause of this condition. Other effects of A-deficiency are upon the surface coverings and linings of the body, for instance, those of the skin and respiratory tract. They become thickened and perhaps invaded by bacteria, as in xerophthalmia, which involves the coverings of the eye. Vitamin A is also generally supposed to assist the body in resisting infection of all kinds.

Absence of vitamin D impairs the formation of bone, in which the bone salt, i.e. the hard mineral part, is laid down on a foundation of living tissue. This process obviously goes on during the whole period of growth, but when we consider that bone is hollow we realise that in order for it to be the same shape when it is large as it was when it was small a process of absorption of bone on the inside has kept pace with a process of deposition at the ends and on the outside. In short, the growth muscles are thrown into action, some simultaneously and some in succession. The proper stimulus is the placing of an object of appropriate shape, size, texture and consistency on the back of the tongue. We know that the most inappropriate objects are sometimes accidentally swallowed, so there is no great precision about the type of stimulus required; furthermore, inappropriate objects such as dry pills can be swallowed voluntarily, i.e. the motor side of the reflex can be set in motion from the cortex. Nevertheless, stimulation of some of the same receptors with a feather, or a prickly bundle of fishbones, or a too large oyster, may induce the reverse process of retching and even vomiting, so we must assume that the swallowing centre is more susceptible to certain combinations of afferent impulses than to others. We may hazard a guess that this is because the ineffective combinations impinge on the centre in such a way as to evoke central inhibition (see p. 63).

In the *stomach*, meanwhile, the secretion of *gastric juice* has started. The myriads of glands opening on to the lining of the stomach are under reflex control, the centre being in the medulla and the initiating stimuli the same as for the salivary glands (fig. 80). This means that the afferent nerves carrying the impulses branch not only to the salivary nuclei and cortex, but also to the nucleus controlling gastric secretion. The efferent nerve is the vagus, and if this is cut no reflex secretion of gastric juice occurs. Unlike the salivary glands the gastric glands are not permanently inactivated by this treatment. The presence of food in the stomach, even when the nerves are cut, leads in about a half an hour to a copious secretion. It seems that cells in the wall of the stomach are sensitive to the presence of food, and that they do not use the nervous system for transforming this irritability into action, but "on their own" make a chemical substance which they transfer to the blood stream. The blood returns via the liver and lungs to the heart, from which it is finally redistributed to the body—and among other places to the gastric glands. These are exquisitely sensitive to the substance added to the blood by the surface cells, and respond by pouring out their secretion.

This seems a clumsy method of communication, but the body makes extensive use of it, and it is not quite so clumsy as it looks. The nerve impulses which travel up the afferent side of the reflex are no different from any other nerve impulse, and the fact that they give rise to a particular result and not to any other result depends on the anatomical termination of the fibres which carry them. The resultant excitation will always follow the same general pathway in the central nervous system, and will finally emerge as nerve impulses in the appropriate efferent nerves. Knowing as much as we do about the flexibility of nervous action, we cannot call this mechanism clumsy, but it is certainly elaborate. Chemical messengers, on the other hand, need no sorting out or special pathways. They fit a certain physiological reaction, such as secretion by the gastric glands, like a key fits a lock. A substance like *gastrin*, the chemical messenger we are concerned with at the moment, can pervade the whole body, yet all parts of the body, with one exception, will be indifferent to its presence. It cannot fail to get to the right destination because it goes everywhere, yet in going everywhere it can do no harm. Such substances are called *hormones*.

Gastric juice contains an important enzyme called *pepsin* which splits up the molecules of protein into smaller, but still considerable, molecules called proteoses and peptones. We remarked on p. 94 that enzymes were very particular about the conditions under which they worked, and pepsin is peculiar in working at a very much higher hydrogen ion concentration (p. 138) than the vast majority of enzymes on which the intracellular processes of oxidation, etc., depend. The necessary conditions for peptic action are fulfilled by the simultaneous manufacture of hydrochloric acid by certain of the cells composing the gastric glands. This is an exceptionally strong reagent for the body to use, and there is much speculation as to how the cells manage to employ successfully its components (hydrogen and chloride ions) without killing themselves either with the acid, or with the equivalent number of (OH) ions which must be left behind. However, they appear to produce the acid with great efficiency, and it mixes with the pepsin secreted by neighbouring cells to form the mixture which is exuded into the general cavity of the stomach The cells lining the stomach are protected in some way from the powerful digestive action of gastric juice, though if they are damaged or divitalised they may become susceptible to it, and a miniature crater may appear in the wall of the stomach—a so-called gastric or peptic ulcer.

Not all parts of the stomach wall secrete active gastric juice; the glands towards the lower end are mostly engaged in producing a mucous secretion.

The outer parts of the stomach wall are composed of sheets of involuntary or smooth muscle (see fig. 17.) which, it will be remembered, has the power of going either into sustained contraction, or of rhythmically contracting and relaxing, quite independently of nervous influences. It is not, of course, allowed to indulge in this independence, but its fundamental nature is important in connection with its nerve supply. Like voluntary muscle, it requires nerve impulses to increase its activity, but unlike voluntary muscle it will not become inert when these impulses cease to arrive (p. 64). It also requires impulses from another source to subdue its activity. Accordingly, we find the stomach wall innervated from both the spinal cord (via the sympathetic nerves) and the medulla (via the vagus nerve) by two independent nerve supplies, the former of a generally inhibitory nature and the latter generally excitatory. Through them co-ordination of movement between different parts of the stomach, and between the stomach and other parts of the alimentary tract, occurs. There is an extensive local network of nerve fibres and cells in the muscular coat of the stomach, and it probably helps in the co-ordination, though very little is known about its function.

The outlet from the stomach, the *pylorus*, is surrounded by a powerful circular band or "sphincter" of smooth muscle which is probably reflexly controlled. During the earlier period of gastric digestion it is strongly contracted. The waves of contraction which can be seen (with the aid of X-rays) sweeping forward in the stomach wall merely serve, therefore, to drive the mixture of food and gastric juice against an obstruction, and although a little may escape, the main effect is one of a thorough churning of the food. This naturally cannot be successful until sufficient gastric juice has been secreted to reduce the consistency of the semi-solid mass which has entered from the mouth, and it is during the penetration of the mass by gastric juice that salivary digestion takes place. Directly hydrochloric acid comes in contact with amylase, it destroys it. The stomach adapts itself accurately to the size of the meal it has to accommodate in virtue of the ability of smooth muscle to assume and maintain any average length.

As digestion proceeds, the opening of the pylorus becomes more and more frequent, and in 2 or 3 hours the stomach has usually completely rid itself of a meal. If the meal is very fatty, however, a chemical messenger called *enterogastrone* is released into the blood stream from the cells lining the duodenum, and this has the effect of delaying the emptying of the stomach by reducing its motility. It appears to have a direct depressing action on the muscle cells. The latter are also under reflex control, and the way in which the numerous factors capable of influencing the emptying of the stomach are finally combined is difficult to describe.

In the *duodenum*, the food meets the secretion of the pancreas which contains a powerful battery of enzymes. *Trypsin* enables protein to be split up almost as far as the stage of individual amino-acids. *Lipase* breaks up fats into the individual fatty acids (still quite large molecules) of which they are composed, and glycerol. *Amylase* converts the remainder of the starch to maltose.

The secretion of pancreatic juice is partly under reflex control, like that of the gastric juice, but it is very largely dependent upon a chemical messenger—the first to be discovered—called *secretin*, which is passed into the blood stream by the surface cells of the duodenum when the products of gastric digestion come in contact with them. When secretin reaches the alveoli in the depths of the pancreas, the cells composing them pour a copious secretion into their ducts.

Another chemical messenger, *cholecystokynin*, acts on the gall bladder (fig. 78) causing it to empty itself of the store of concentrated *bile* it contains. At the same time, secretin exerts a similar action on the cells of the liver to that which it has on those of the pancreas and they manufacture more bile. This mixes with the gall-bladder bile and is discharged into the duodenum together with it and with the pancreatic juice (fig. 78). Bile is a favourable medium for the enzymes of pancreatic digestion as a whole, but is particularly important for fat, which fragments under its influence into millions of minute droplets with an enormous combined surface, instead of remaining in large globules with a relatively small surface. We can guess what this *emulsion* looks like, because fat is distributed in exactly the same fashion (though not by the agency of bile) in milk. The surface thus created allows not only the lipase to get at the fat, but enables certain components of the bile to combine with the fatty acids to form a temporary chemical association which helps them to remain in solution, and to penetrate the surface of the absorbing cells of the small intestine. The chemical messenger cholecystokynin is evoked chiefly by the presence of fat in the duodenum.

In the remainder of the *small intestine*, the contents of the gut meet the final batch of enzymes which complete the degradation of proteins to amino-acids, and maltose and other carbohydrates to glucose, galactose and fructose (see p. 177). The intestinal juice is secreted by multiple surface glands like those of the stomach, but it is evoked by any object placed in the intestine even when the connection of the intestine with the central nervous system has been severed. It is thought to depend on nerve impulses which come, not from the central nervous system, but from branches of one of the local nerve networks in the intestinal wall. Excitation is thought to be transmitted to the network by fibres arising in the surface cells. A nerve path like this, with afferent and efferent parts, but no direct connection with the central nervous system, is a sort of local or outlying reflex arc which the more slowly acting and primitive mechanisms of the body sometimes employ.

The movements of the small intestine. This in itself is a very interesting subject, but it would be inappropriate for us to discuss it at length in a book of this size. Like the stomach, the wall of the intestine is largely composed of smooth or involuntary muscle (fig. 17). In the outer sheet, the fibres run longitudinally, and in the inner sheet circularly. There is also a network or *plexus* of nerve fibres and cells in close association with the muscular coats, and it co-ordinates the movement of adjacent segments of the tube with each other. We know this, because the waves of contraction in the muscle coats are so organised as to pass the contents of the tube in a forward direction, and this progression can be seen to continue in animals in which the local plexus has been completely isolated from the central nervous system by severing all the nervous connections. If the local plexus itself is thrown out of action by applying nicotine to it, a drug which prevents the passage of excitation across synapses, then the forward movement or *peristalsis* ceases.

Although the gut *can* manipulate its contents independently of the central nervous system, it is unlikely that it ever does so during normal life. The local mechanism is itself under the control of the vagus nerve, which rises from the medulla, and sympathetic nerves from the spinal cord. The former tends to speed up the passage of food, and the latter to retard it. The degree of movement depends largely on the balance of impulses conveyed by these two innervations.

Other muscular movements take place which are probably independent of nervous activity. It will be recalled that smooth muscle has the power of rhythmic contraction, and in the gut this serves to keep the contents well mixed.

Absorption

The products of protein and carbohydrate digestion—amino-acids, glucose, fructose and galactose—are transferred by the cells covering the villi directly into the capillary blood vessels which lie beneath them (fig. 78). They must pass through the tissue fluid on the way, but their molecules easily cross the thin capillary walls, and no local accumulation is allowed to occur. Fat is not removed so simply. To begin with, the molecules of fatty acid in the intestine remain obstinately large, and they are not readily soluble in water. We have remarked that this initial difficulty is overcome by their forming some kind of soluble compound with certain constituents of the bile, and this gets them into the interior of the cells. Here they are deserted by the bile salts, and not only come out of solution, but appear as small droplets of fat. It is assumed that they have recombined with glycerol in order to do this, but there is some evidence that undigested fat may, with the assistance of bile, get so far. The remainder of the process is something of a mystery. The fat is transferred across the opposite cell boundary into the tissue fluid, but fails to enter the capillaries. An impasse is avoided by an alternative path into the bloodstream which we have so far not mentioned.

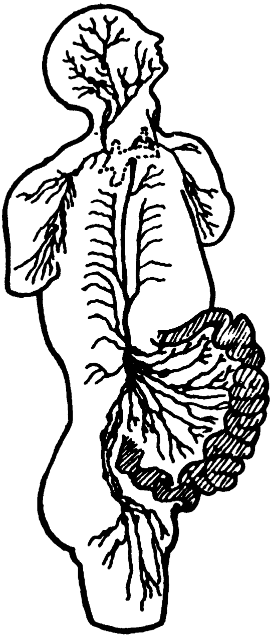


FIG. 81. Diagram of the main lymphatic blood vessels with the intestine displaced so as to show their arrangement in mesentery. The dotted lines at the junction of the neck and chest represent the large veins into which the lymphatic system drains (after Dalton, *Human Physiology*, 1864).

The Lymphatic System

The balance of the interchange of fluid between tissue fluid and capillary blood vessels is not so perfect as we described on page 102. Some of the fluid which is forced through the capillary walls by the pressure behind it is not drawn back by the attractive power of the plasma proteins. It has to find its way back into the blood stream by an alternative channel. This is provided by a second system of vessels whose capillaries start in the tissue spaces, gradually become organised into definite channels, and finally converge to form well-marked vessels, something like veins, which contain valves. Instead of blood, these vessels contain a clear fluid, the origin of which we have described, and which is called *lymph*. The lymph vessels from the limbs, trunk and head eventually emerge into three main vessels, two of which, each serving one arm and half the head, are symmetrical and enter the large veins at the root of the neck. the third, which drains the lower limbs and the trunk, including the digestive tract, runs up the inside of the chest at the back, and joins the left one of the pair we have already described and enters the veins at the root of the neck on the left side (fig. 81).

Elephantiasis, a disease met with in some foreign countries, is mainly due to the lymphatic vessels of a limb becoming blocked by a parasite, with the result that its size is vastly increased on account of the fluid which enters its tissue spaces, yet cannot leave. Obstruction to the lymphatic drainage of a limb renders it uniformly tense, and cells which were formerly in apposition are presumably slightly separated from each other by fluid. On account of some such disturbance of local relations plus the effect of repeated inflammation, or for a reason we do not understand, the skin and underlying tissue thicken to a surprising degree, and the limb becomes genuinely increased in size, as distinct from being merely "blown up". Lymphatic blockage may, of course, occur from other reasons, and conditions more or less resembling elephantiasis are by no means unknown.

The lymphatic system of drainage is, therefore, something more than a mere luxury, and in the intestines it furnishes the route for the absorption of fat. If a piece of intestine be lifted up through an incision through the anterior abdominal wall, it will be found attached to the posterior wall of the abdominal cavity by a sheet-like structure called the *mesentery*. This is almost transparent, and when spread out (fig. 82) the blood

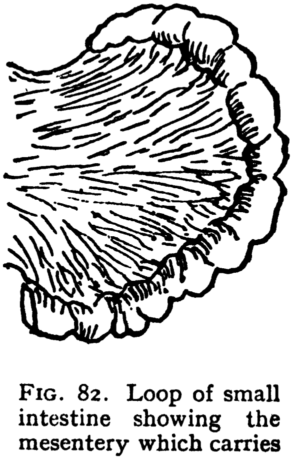


FIG. 82. Loop of small intestine showing the mesentery which carries blood vessels, lymphatics and nerves.

vessels it carries can be clearly seen. After a meal of fat, the lymphatic vessels can also be seen on account of the milky appearance which the otherwise clear lymph assumes when laden with countless droplets of fat.

CHAPTER XVI

THE UTILISATION OF THE FUEL

The fate of glucose

FRUCTOSE and galactose appear to be converted into glucose by an internal rearrangement of their molecules on their way from the inside of the gut to the blood stream, so that the sugar of the blood is glucose. It is an important constituent of the blood plasma. If it is *deficient,* the cells of the nervous system begin to act abnormally: great mental anxiety is experienced, unco-ordinated discharges of nerve impulses cause sweating and perhaps convulsive muscular movements, and consciousness is finally lost. *Excess* of blood sugar leads to its " overflow " into the urine (see Chapter XVII), with the consequent wastage of valuable food material, and beyond a certain point also leads to a loss of consciousness, familiar as " diabetic coma ". In diabetes, however, the *cause* of the raised concentration of glucose in the blood rather than the concentration itself is important.

If it were not for the liver, the body would be flooded with glucose after meals, much of which would escape in the urine, and we should experience a lack of it between meals. One of the tasks of the liver is to keep the concentration of blood sugar constant, and it carries a store of glycogen (" animal starch ", see page 177) in its cells which, between meals, it breaks down to glucose at a rate just sufficient for this purpose. If the rate at which the tissues of the body remove glucose from the blood increases, so the rate of breakdown of glycogen in the liver increases. After a meal, the liver seizes the glucose presented to it in the portal vein, and hurriedly builds it up into glycogen to replenish the store, attempting meanwhile to continue doling out glucose to the blood at the same rate as before.

. This automatic levelling of the blood sugar concentration by the liver is an excellent example of the kind of mechanism which is necessary to keep the internal environment of the body constant. One must picture each liver cell sensitive to the glucose concentration of the fluid which bathes it: if this is greater than 100 mg. per 100 cc., glucose is abstracted and built into glycogen, while if it is less, glycogen is broken down and glucose is secreted into the blood. We shall see later that this two-way mechanism is profoundly influenced by events in other parts of the body, and is under the control of a number of positive and negative influences, in much the same way as the synapses of a nerve centre are influenced by excitation and inhibition coming in from all sides.

The critical reader is already asking what happens during starvation? If he could mobilise the requisite knowledge, he would argue something like this: The liver of a 70 kgm. man is about 3.3 per cent of his body weight and may contain about 5 per cent of glycogen. This represents a store of about 100 gm. of carbohydrate. Muscle cells also store glycogen (p. 92), but only about 1 per cent of their weight. If the muscles constitute half the weight of the body, they represent a store of a further 350 gm. of carbohydrate. Now if the energy production of the body (say 3000 kilocalories per day) is occurring exclusively at the expense of carbohydrate, 750 gm. per day will be needed (see p. 157), i.e. the glycogen stores will be exhausted in less than a day. It is common knowledge that men have survived starvation from more than a fortnight, provided they have been able to drink, and according to what we have said about the blood-sugar level, some glycogen must have been preserved in the liver for that length of time. There is no evidence that the glycogen of muscles can supply glucose to the blood; it is there to furnish fuel for the muscles, and represents a drain on the blood.

It seems unlikely that with the onset of starvation, of which the body might not even be aware for about a day, the habits of the tissues would suddenly change. In order to conserve the few hours' store of liver glycogen, the muscles (and other tissues) would immediately have to stop using carbohydrate as fuel, so that their own stores would not diminish, and no more glucose would have to be diverted from the blood into them. The blood-sugar level would then not be endangered. Nothing of this kind, in fact, happens. When the nitrogen has been split off from the amino-acids, the remainder of the molecule contains carbon, hydrogen and oxygen, frequently in a form which the liver can build up into glycogen. Such amino-acids in the food which can be used for this purpose are so used by the liver, so that its normal store of glycogen is by no means all built up from "prefabricated" molecules of glucose. The question naturally follows, how this can possibly help in starvation, since no food of any kind is being eaten. The answer is that the body itself is a great store of protein (compare page 23).

"Wear and tear" of the tissues is constantly in progress. This means that, bit by bit, the protoplasm of cells is disintegrating. Its protein component, for some reason connected with the breakdown and loss of mutual protection between the molecules of the living complex, becomes exposed to enzymes in the cell which have a digestive action. *Amino-acids are constantly liberated into the blood stream from the tissues.* It is equally true to say they are constantly being taken up, and the converse process of building up new protein and new protoplasm is perpetually going on. The tissue fluid and blood represent a pool of amino-acids from which the cells draw what they need, and into which they cast what is useless to them; intermittently, it is replenished by a batch of amino-acids from the food.

During starvation, the pool of amino-acids is still there—indeed, the breakdown of the tissues is probably accelerated—and these precious molecules are used to furnish energy. Processes of repair in the cells languish, though some tissues like the brain and heart seem to exercise a priority over the available supply and maintain their weight fairly well. But the voluntary muscles waste rapidly. Their substance is being used partly to maintain more essential organs, and partly as fuel. One of the most important ways in which amino-acids can be utilised as fuel is by their conversion, where possible, into liver glycogen. In this way the cells finally receive at least part of their food in the familiar form of glucose, and the level of the blood sugar concentration is kept constant.

The fate of the amino-acids

We have little more to say on this point. Those amino-acids whose non-nitrogenous part is unsuitable for conversion into glycogen can nevertheless be oxidised directly in the liver, or elsewhere, and used as fuel, so we may state that the fate of amino-acids is to be used as fuel, or to be built up into protein in the way we have just described. A few details remain to be filled in.

All the amino-acids of the food must run the gauntlet of the liver, and a proportion of those liberated from the cells of the body into the blood must pass through the liver every time the blood circulates. Some of the amino-acids, particularly the "essential" ones (p. 175), entering the liver escape from it—at all events, the blood leaving the liver is not free of amino-acids—and these circulate in the blood to all tissues of the body.

There is a possibility that the liver cells can use their own protoplasm as a protein (i.e. amino-acid) store in much the same way as they use glycogen as a source of glucose. Be this as it may, a high proportion of amino-acids entering the liver by the portal vein fails to get through into the general circulation. It represents those destined for fuel, and introduces us to an important function of the liver, namely, the de-amination of amino-acids. The term is almost self-explanatory, and means that the nitrogen-containing part of the molecule, which is incapable of oxidation by the mechanisms available to the body, is split off, leaving the rest of the molecule free to be oxidised or converted into glycogen. The detached nitrogen is converted into unoxidisable but very soluble substance, *urea*, which is carried away from the liver in the blood. So far as we know, it is useless to the body, and can be present in high concentration without doing it any great harm. In healthy persons it is not allowed to accumulate and is removed through the kidneys (Chapter XVII).

The fate of fat

Fat circulates in the blood for many hours after a meal. Some of it is doubtless used to repair wear and tear in the tissues and to restore that part of their protoplasm of which fat is an integral part. Some of it is used as fuel and oxidised. The remainder is stored. The fat stores represent the most important depot of fuel which the body possesses, and during starvation they have a great protein-sparing and therefore tissue-sparing effect. Fat not only yields more calories per gramme than the other foodstuffs, but it is undiluted with water. 100 gm. of fat will supply as much energy as 1500 gm. of muscle, because only about 15 per cent of the latter is protein—i.e., about 225 gm.—and each gramme of protein is worth only 4 kilocalories as against 9 kilocalories for a gramme of fat. When the body loses muscle, it loses active tissue; when it loses fat, it loses mere fuel.

Fat is stored in cells which lie among the feltwork of fibres which support the skin and which fill in various spaces between organs and all kinds of anatomical structures. There is a good deal, for instance, round the kidneys. Each storage cell is so distended by its globule of fat that the protoplasm is reduced to a thin layer, with a bulge where the nucleus lies (fig. 83). In obese persons the fat cells are numerous and closely packed, and may form a layer inches thick beneath the skin. Such people also have a thick pad hanging down inside the abdominal cavity in front of the intestines. A certain amount of fat is stored in the liver cells.

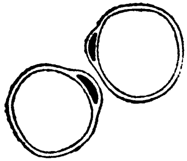


FIG. 83. Fat cells.

Water and minerals

Water passes rapidly through the stomach when this is empty, and it is absorbed into the blood within a matter of minutes after entering the small intestine. From the blood stream it is distributed among the fluid compartments of the body in such a way that none of them contains a " stronger " solution than another (p. 179). Many other substances pass through the cells of the intestinal villi with great ease; sodium chloride and bicarbonate are examples, and numerous drugs with quite large molecules penetrate readily. Even insoluble substances like aspirin get into the blood stream quickly when taken by the mouth.

There is something peculiar, however, about the cells lining the gut. The nature of the barrier which they interpose is one of the great problems of biology. We are familiar with barriers which will pass all molecules below a certain size and none above it, and we know that some molecules in solution are more mobile than others, and tend to negotiate obstructions more readily than their fellows. But the selection of molecules for transmission from gut to blood stream is carried out by more complicated methods. For instance, although glucose and fructose and galactose are absorbed, numerous other sugars with molecules of exactly the same size, and differing from these three no more than they differ from each other, are rejected. Magnesium sulphate (Epsom salts), which resembles sodium chloride much more than many of the substances which can cross the barrier, is firmly kept in the alimentary canal. If it is taken in concentrated solution it withdraws water from the cells of the gut, which in turn abstract water from the blood stream, until the solution of magnesium sulphate is approximately as dilute as the proper body fluids. The increased bulk of the intestinal contents stretches the muscle coats and thereby stimulates them to greater activity, and the mass of fluid is hurried on. That is why magnesium sulphate acts as an aperient, and a number of other poorly absorbed salts act similarly.

All the minerals which are found in the body are ultimately replenished from the food, but they include some which are absorbed only with difficulty, such as iron and calcium and phosphorus. The absorption of calcium is said to be rendered easier by the bile (compare the fatty acids), and the presence of vitamin D may also influence the permeability of the cells of the villi to both calcium and phosphates. Lack of absorption may sometimes be due to " accidental " causes; for instance, cereals often convert calcium into an insoluble and unassimilable form.

CHAPTER XVII

THE EXCRETION OF WASTE

When the contents of the small intestine reach the end of it, all the useful material has been absorbed from them with the exception of some water. They reach this point 4 to 6 hours after a meal, and are periodically discharged into the *large intestine* (fig. 52). The lowest bag-like portion of this is the *caecum*, with the blind *vermiform appendix* of unknown function attached to it. The fluid and debris from the small intestine fill up the caecum and the *ascending colon*, the next part of the large intestine, and for the remainder of their stay become known as *faeces*. The faeces move very slowly up the ascending and along the transverse colon and become semi-solid owing to the absorption of water from them. They are at first composed of those portions of the food which are insoluble in the digestive juices, together with dead surface cells from the 8 yards or so of alimentary tract through which they have come, but in the large intestine the bodies of millions of bacteria are added to them, and finally constitute an appreciable proportion of their bulk. In herbivorous animals, the stalks and leaves of plants, although not attacked by the digestive juices, are broken down by the bacteria of the large intestine into useful sugar. In man this does not occur to any useful extent, though the bacteria do find odds and ends of materials which are useful to them as food, and which they break down, often with the formation of evil-smelling compounds. So long as they stay in the large intestine, these bacteria are quite harmless.

Although *cellulose*, of which the skeleton of plants is built, is of no food value to man, it is an important part of the diet on account of the bulk it lends to the faeces. When the ascending and transverse colon are full, or nearly full, a powerful propulsive movement occurs which transfers the contents bodily into the pelvic colon. If the faeces lack bulk, this and subsequent forward movements may be delayed, leading to uncomfortable distension from the gaseous products of bacterial putrefaction, and perhaps to a feeling of illness from absorption into the blood of poisonous soluble substances.

From about the middle of the transverse colon the vagus nerve from the medulla ceases to supply the colon, but its place is taken by a nerve from the very last part of the spinal cord. The nerve supply is still double, the colon sharing with other parts of the gut the innervation from the higher parts of the spinal cord. It is a curious but well-established fact that visceral structures remote from the medulla get that part of their nerve supply which acts in the complementary sense to the sympathetic from the last or *sacral*, region of the spinal cord. Nerves innervating glands and smooth muscle (including some blood-vessels) and *arising in the brain stem and the sacral cord* are often referred to as " parasympathetic ". The reason is that they so often exert an influence different from that of the sympathetic supply to the same organs, though it must be remembered that the two work in harmony. It is important to remember also that although organs supplied by parasympathetic nerves are nearly always supplied by sympathetic ones, the reverse is not true. In particular, most of the blood vessels of the body have a sympathetic supply, but comparatively few have a parasympathetic supply (cf. p. 68).

From the pelvic colon, the faeces are passed at intervals—usually daily, but sometimes more or less frequently than this—into the *rectum*, the last part of the large intestine. It is the duty of the rectum to expel its contents to the exterior, but it cannot do this automatically in the way that the food and faeces have been moved so far. Although the muscle of its walls is " involuntary ", it is partly under control of the will. Unfortunately, this is a " one-way " control. The rectum can be prevented from emptying itself, but it cannot voluntarily be emptied. We say this is unfortunate because the distension of the rectum by faeces leads not only to a natural tendency to emptying, but also to a definite sensation, and if this sensation is ignored it passes off. Its disappearance is an indication that the distension has disappeared also. This may seem impossible, but as we have frequently stated, smooth muscle can assume almost any length, and that of the rectum may " adapt itself " to its contents. Instead of having muscle fibres of a certain length stretched and trying to return to their original length, we have fibres just settling down to the new length. If the muscle of the rectum does for some reason try to contract again, the desire to defaecate returns, but this may not happen until a fresh load of faeces has been thrust into it from the pelvic colon. Neglect of the call to defaecate in all probability slows up the passage of faeces through the whole of the large intestine, and many persons believe that this, together with the lack of bulk of the faeces on a civilised diet which also makes them move more slowly, is the cause of a great deal of ill-health. This is probably true, and the remedy is to correct these two defects, rather than to flog the bowel into activity by purgatives and patent medicines. It is also worth remembering that large intestines, like their owners, differ. A frequency of evacuation which might mean constipation for one person is normal for another.

The Kidneys

In the note about the kidney on page 111 we stated that its task was to eliminate from the blood and tissue fluid, i.e. from the internal environment, certain substances in solution. Some of these are waste products, but some do not fit this description. Even an innocent substance like sodium chloride (common salt), which is an essential constituent of the diet, can be embarrassing to the body if its amount is not controlled. We have referred several times to the " strength " of the body fluids in dissolved substances, and we have seen how a " strong " solution will withdraw water from a " weaker " one across any of the cell walls in the body and therefore across a membrane composed of cells. Now the internal life of the working cells of the body seems to proceed best when the strength of the intra-cellular fluid is equal to that of a solution of 0.9 gm. of sodium chloride in 100 cc. of water. If the extra-cellular or tissue fluid is stronger or weaker than this, molecules of water pass out of or into the cells to make the internal and external strengths of the solution equal. In other words, the cells promptly suffer from any change in the strength of solution in their surroundings—the internal environment of the body.

If one day we eat an abnormally large quantity of salt, this passes readily into the blood and thence into the tissue fluid. Water is withdrawn from the cells, and all the fluids in the body become stronger solutions than they were before. This state of affairs can be corrected in two ways—either by getting rid of the salt or by drinking enough water to dilute the body fluids to their original strength. The obvious solution is to excrete the salt, and this is what the body does with the help of the kidneys. In certain diseases the kidneys are incapable of doing this, and we then see the effects of the alternative method. There is more fluid in the body than there was before, and the more salt is taken, the more water is retained. The body becomes " water-logged " or " dropsical " or " oedematous ", particularly in the more dependent parts to which the fluid tends to gravitate.

In addition to excreting soluble waste products, therefore, the kidney regulates the strength of the solutions which permeate the body, excreting the appropriate quantities of water or salt. It is instructive to drink a quart of water and collect all the urine which is passed in the next two or three hours; the flow will be copious, the urine dilute and practically colourless, and the total amount almost exactly the same as the volume of water drunk.

Besides exercising these two functions, the kidney helps to regulate the hydrogen ion concentration of the blood and tissue fluid. We remarked on page 139 that this was not determined by the presence of any one substance, but was the upshot of several substances being simultaneously in solution. Its final value can be modified by altering the concentration of one or more components of the blood plasma, and the kidney helps to keep it constant by doing this.

Countless experiments have been performed by three generations of physiologists in order to find out how the kidneys work, but many of their conclusions are now sufficiently well established to be stated in a few words. As with the cells lining the intestine—and indeed with any cells producing chemical products of a different nature or in a different concentration from those presented to them—the mystery of the internal cellular mechanism remains.

Each kidney consists of about a million tiny tubes or ***tubules*** which are very long compared with their diameter, and which are for the most part lined by cubical cells, i.e., cells with plenty of protoplasm which might be expected to do important work. The lower ends of the tubules run into ducts, and these into bigger ducts, and so forth. The fluid which is collected by these ducts is finally led away from the kidney in a single wide tube with muscular walls known as the ***ureter***. The other ends of the tubules lie fairly near the surface of the kidney, and are blind. In fig. 84*a* is a sketch of what was probably Nature's first attempt at one of these blind ends—a little balloon with a very thin wall composed of flake-like cells, something like those of the lung alveoli. In the modern version, the top of the balloon has been pushed downwards as in fig. 84*c* to form a cup, ***Bowman's capsule***. A short arteriole enters the capsule and breaks up into a sheaf of capillaries—the *glomerulus*—which completely fill the outer cup. They join up again to form another arteriole (a unique arrangement found nowhere else), and this second arteriole proceeds to split up in a more conventional and leisurely way into ordinary capillaries, which supply the tubules along their length and finally gather up into venules and veins

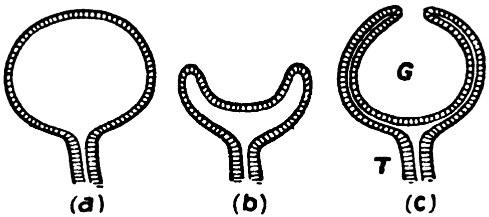


FIG. 84. An imaginary sketch of the evolution of the upper end of the kidney tubule.

The space G is packed with capillary blood vessels and de-proteinised plasma is filtered into the tubule T.

We described on page 102 how the head of pressure behind the blood forced the water of the plasma, with all its dissolved constituents except the plasma proteins, through the walls of the capillary and into the tissue spaces. Exactly the same thing happens, but with more precision, in the glomeruli of the kidney. In the ordinary tissues a certain amount of protein does get through into the tissue fluid, and both red and white blood cells, particularly the latter, can squeeze through the capillary wall by prising apart the plate-like cells of which they are composed. In the glomerulus, the barrier of capillary-with-capsule keeps back all formed elements and all the plasma protein molecules. It is, in fact, the kind of sieve-like membrane we mentioned on page 203 which lets through all molecules below a certain size and none above it. The coloured protein haemoglobin, which confers the ability to carry oxygen upon the red blood cells, is just small enough to get through. If, by some mischance, red cells are destroyed in the blood and haemoglobin liberated into the plasma, it finds its way into the kidney tubules, passes to the exterior in the urine and is lost. On the way it is altered chemically by the other constituents of the urine and changes colour—hence the name " blackwater fever " for a disease in which this occurs. If the glomerulus is damaged by disease it may let through molecules of the protein *serum albumin*, which are the smallest of those belonging to the plasma proteins.

By exquisite microscopic and chemical technique it has been possible to puncture the glomeruli of frogs and collect and analyse a little of the fluid which filters on to the tubular side of the capsular membrane. It has the same composition as blood plasma without its proteins. The glomerulus is therefore a mechanical sieve, of molecular dimensions, through which molecules of water and all the other components of the plasma except protein are forced by the pressure of the blood. As the main artery to the kidney is short and wide, and the glomerular arterioles are also short, the pressure in the glomerular capillaries is higher than in most of the other capillaries of the body. Nevertheless, the amount of fluid which can be filtered off is limited. The flow of blood is too fast for more than a fraction to be removed, and in any case the attractive power of the plasma proteins for water would ensure that a certain amount was left behind. In the limit, of course, any mechanism whereby so much fluid was filtered off that the blood " went solid " in the glomerular capillaries could not possibly work. About one-sixth of the plasma is removed during its passage through the glomerulus.

It has been calculated that in the course of a day the two kidneys working together remove about 180 litres of fluid from the blood in this way.[1] Since this is more than twenty times the total volume of blood in the body, and since we drink on the average only from one to two litres of water a day, it follows that most of this enormous volume is returned to the blood stream. The only outlet for the fluid is via the two ureters to the urinary bladder, and thence to the exterior, and the volume of urine we excrete in a day is only about one-and-a-half litres. Somewhere between the glomeruli and the ureter about 99 per cent of the filtered plasma has been returned to the blood. This restitution is made by the cells lining the tubules as the fluid trickles through them, but whereas most of the water and all the glucose is returned, this is by no means true of the other constituents of the urine. Only about 80 per cent of uric acid, 40 per cent of urea, 30 per cent of sulphate and a negligible amount of creatinine are returned to the blood stream.

We have not encountered some of these substances before, but that does not affect the point we wish to make. Sulphate is the form in which the sulphur of certain amino-acids is excreted; uric acid is a nitrogen-containing product of the disintegration of the kind of protein—nucleoprotein—found in the nuclei of cells; creatinine is a nitrogen-containing substance from the metabolism of muscle cells.

[1] A substance, *inulin*, is injected into the blood stream, time allowed for it to mix, and its concentration measured in a sample of blood. It is known to pass through the glomerular capsule with the other constituents of the plasma, and not to be removed from the tubules during the whole of its passage through them. The amount which appears in the urine during a given time therefore represents a definite volume of plasma and an equal volume of glomerular filtrate. The arithmetic is complicated by the fact that the plasma concentration falls as the inulin is removed from it, but allowance is made for this.

The urine is obviously going to be much more concentrated than the blood plasma, but more so in respect of some constituents than others. Thus a given volume of urine may contain 100 times the weight of creatinine found in the same volume of plasma, but only 60 times the weight of urea and 20 times the weight of uric acid.

From what we have said of the tendency of body fluids to equalise their concentrations, it will be realised that the kidney cells must work hard to prevent these substances returning with the water which is passed back into the blood. What the discrimination between substances means in terms of work it is hard to say, neither do we know what it is that determines that one substance shall be less readily reabsorbed than another. There are variations in the treatment of the same substance from day to day; for instance, if we stop eating salt its concentration in the plasma will scarcely be affected, yet it will disappear altogether from the urine. This means that the whole of the salt in the glomerular filtrate has been returned by the tubules to the blood. In the ordinary course of events, the concentration of chloride in the urine is equal to, or perhaps double that, of the plasma; it fluctuates a good deal. Phosphates likewise fluctuate, being concerned with the hydrogen ion concentration of the blood.

One of the most striking events which occurs in the kidney is the complete return of glucose to the blood. There is normally about 0.1 gm. of this substance in 100 cc. blood, and the glomerular filtrate contains the same proportion, but every scrap of it is removed during the passage of the fluid along the tubules. If the concentration of glucose in the blood rises to 0.2 gm. per 100 cc., as it may do in diabetes mellitus, the tubule cells cannot manage to salvage all of it, and a proportion leaks away in the urine.

There are other limits to what the kidney can do, as can be demonstrated by giving it excessive quantities of one substance to deal with. We have seen, for instance (p. 207), that a litre of water is promptly and efficiently excreted soon after it is drunk. But in spite of the great dilution of the urine, the *total* of the solid constituents in solution during the excessive flow is rather more than would have been excreted during the same period in urine of normal concentration. In rejecting a certain amount of the water presented to them, the tubules have had to let go some of the solids they would otherwise have returned to the blood. If an excessive amount of salt is eaten, a greater proportion than usual is rejected by the tubules, but when the salt rises to a certain concentration in the tubular fluid the cells must either start admitting it or stop taking up so much water; the attraction of the salt for water defies even the power of the tubule cells to separate them. The usual result is that an excess of salt is eliminated from the body by the kidneys, but only at the expense of some water which would otherwise have been reabsorbed. The total volume of urine is increased. This result is much more marked in the case of urea which, if given by the mouth, provokes a copious flow of urine.

The Urinary Bladder

The urine which is formed by each kidney flows into the corresponding ureter, which is a long tube ending in the urinary bladder (figs. 54, 85). This is a hollow organ lined by an epithelium something like that covering the skin. The remainder of the wall is composed of smooth muscle fibres collected into bands which run in all directions and form a complete investment of the organ thicker in some places than in others. The ureters pass so obliquely through this muscular wall to their openings in the interior that their lower ends are squeezed shut. To overcome this obstacle the urine which they contain must be forced past it in some way.

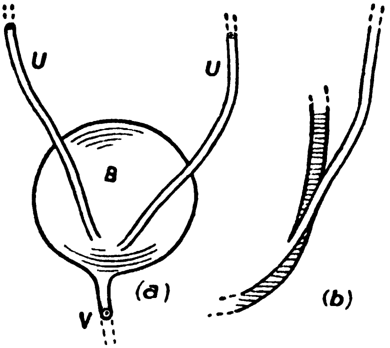


FIG. 85.

(*a*) B, urinary bladder from the back. U, ureters leading into it. V, opening leading via the urethra to the exterior.

(*b*) Bladder wall cut to show method of opening of ureter.

This is effected by a constriction of the ureter (also surrounded by smooth muscle) which starts near the upper end and travels down like a wave. It recurs every few seconds and forces jets of urine into the bladder. The latter becomes larger and larger as it fills, and for a time the muscle in its wall gives way easily, so that very little tension is set up. Ultimately, however, the pressure inside it increases. On account of the filling mechanism we have described, it is still possible for urine to be forced into the bladder and for the pressure inside it to rise further and further. It can easily be seen from fig. 85*b* that the more distended the bladder becomes the more firmly are the ends of the ureters squeezed, therefore the pressure which is set up is not transmitted backwards up the ureters where it might stretch and injure the kidney tubules. The protection thus afforded to

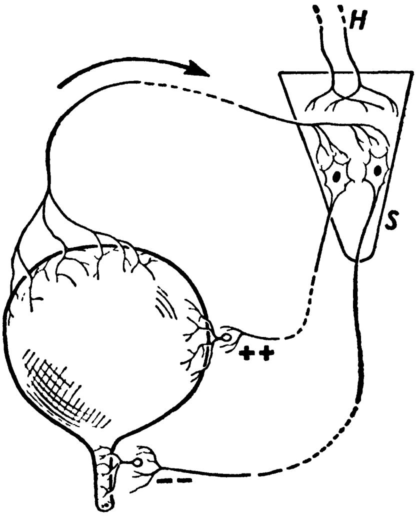


FIG. 86. Reflex control of the bladder.

The positive and negative signs indicate that when the wall of the bladder contracts, the muscle guarding the opening into the urethra relaxes. This is a kind of reciprocal innervation in which the inhibition is peripheral. Central inhibition does, however, occur in the spinal centre, S, via the nerve fibres, H, from higher centres.

the kidney is even more important when the muscle of the bladder begins to contract, because under these conditions quite high peaks of pressure are attained.

By studying persons suffering from spinal injuries, and by means of other experiments, it has been found that when the pressure in the bladder rises to a certain point impulses are set up in afferent nerves starting in the bladder wall and going to the spinal cord. There they excite motor centres, so that impulses are passed down nerves which are capable of throwing the muscular wall of the bladder into contraction. These nerves come from the lowest part of the spinal cord, belong to the sacral parasympathetic division (pp. 68, 205), and pass their excitation to outlying nerve cells which finally relay it to the muscle cells. Nerves from the same source supply the muscle controlling the exit from the bladder and cause this simultaneously to open. The final result is, of course, that the bladder is emptied (*micturition*) and a stream of urine is forced out into the urethra and thence to the exterior (fig. 86). This fundamental mechanism operates unchecked in very young children, but not in adults. The centres in the lower part of the spinal cord gradually come under the control of cells higher in the nervous system, some of which are certainly in the cerebral cortex. These cells send down impulses inhibitory to the centre and therefore capable of neutralising the effect of the excitatory impulses being sent in from the bladder itself.

There is another addition to the purely spinal reflex mechanism with which everyone is familiar, namely, a sensation which cannot be described in terms of the ordinary sensations of touch, temperature, light, sound, taste, pain, etc., but which we only know in the form in which the cerebral cortex interprets it for us—a desire to empty the bladder. It is, however, undoubtedly due in the first place to stretching of the bladder wall and to impulses transmitted upwards by nerve fibres which are branches of, or associated with, those carrying the afferent impulses initiating the reflex mechanism. The intensity of the sensation is proportional to the difficulty of maintaining inhibitory control over the reflex. In its extreme form it may be transformed into actual pain, for instance, as a result of mechanical obstruction to the urethra, and will then be more severe during the efforts of the bladder to expel its contents.

Although all but the final stages of the filling of the bladder are normally quite unconscious, it has been proved that the inhibitory control by the cortex, which is also unconscious, can be withdrawn by an effort of will and the emptying reflex allowed to operate. It is possible that the cortex can actually send impulses down to the spinal centres which increase their excitability. By one or both of these devices, i.e. removing the inhibition or initiating actual excitation, micturition can be brought about. It is an interesting fact that although the bladder is to this degree under voluntary control, no degree of conscious *muscular* effort, in the ordinary sense of the words, will either maintain inhibition when the desire for micturition is strong, nor bring about emptying of the bladder when sensation is absent. The control is exercised by making a decision either to micturate or not to micturate as the case may be, and we are unable to describe it in more precise terms. The effect of these voluntary decisions on the pressure inside the bladder (i.e. on the degree of contraction of its musculature) has been very clearly demonstrated (fig. 87).

The bladder has been known to burst from over-distention, although this can only occur under abnormal circumstances. Normally the reflex mechanism passes beyond voluntary control before an such catastrophe becomes imminent. It is obvious, however, that over-distention of the bladder can occur as a result of mechanical obstruction to the urethra and it may also result

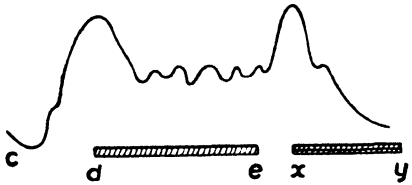


FIG. 87. Record of pressure inside the bladder over a period of about 2 minutes.

At *c* the subject decided to allow his bladder to empty, but at *d* changed his mind and made a certain effort of restraint until *e*, which was then relaxed. He then made a strong effort of restraint from *x* to *y*. This shows the effect of higher centres on the centre controlling bladder movement.

from spinal injuries in which the bladder is "paralysed"; that is to say, the reflex thrown out of action and the exit from the bladder tightly closed. Since connections with the cerebral hemispheres of that part of the spinal cord controlling the bladder are probably interrupted in the latter circumstances, the patient experiences no corresponding sensation.

The abdominal muscles

The abdominal cavity, in which the organs of digestion and excretion and glands like the liver and pancreas are contained, is closed at the top by the dome of the diaphragm (a sheet of muscle, see p. 151) and on its anterior aspect by other striped muscles arranged in sheets so that the direction of the fibres in one sheet is roughly at right angles to the direction in the underlying one. These muscles are attached to the bones of the spinal column, ribs and pelvis, which are the only bony support for the abdominal contents. There is no air in the abdominal cavity between the outer surface of the coils of the intestine, the surfaces of the liver, etc., and the inside surface of the abdominal cavity. There may be a little fluid to lubricate the movement of these structures over each other, as in the case of the two layers of the pleura (p. 150), but this can scarcely be said to occupy any space, and the abdominal cavity is completely filled by the organs we have mentioned. Consequently, as was pointed out earlier, when the dome of the diaphragm descends during breathing, the abdominal contents are pushed outwards and room must be made for them by a relaxation of the other muscles of the abdominal wall. The higher centres which cause rhythmic contraction of the diaphragm are equally responsible for rhythmic relaxation of the abdominal muscles. The impulses which they then send to the motor centres controlling the latter muscles have an inhibitory effect. This type of mechanism is often described as "reciprocal innervation", and it is fundamentally the same as that which determines that when we bend up (flex) a limb the centres controlling those muscles which would be used in stretching (extending) the limb shall be inhibited (p. 153).

It is obvious that if the muscles of the diaphragm and of the anterior abdominal wall contract simultaneously instead of alternately, the contents of the abdomen will be subjected to pressure. This actually happens during the acts of defaecation and micturition and materially assists in the emptying of the hollow organs concerned. It is, however, quite insufficient to bring about either of these acts in the absence of the proper reflexes controlling the organs themselves.

It has often been stated that vomiting is entirely dependent on the simultaneous contraction of the diaphragm and abdominal muscles, the stomach remaining inert. The writer, however, was once fortunate enough in the course of watching an abdominal operation in which the anterior abdominal wall was opened and therefore incapable of exerting pressure, to see the stomach of a patient contract tightly into a ball and forcibly eject its contents. Single observations of this kind are notoriously unreliable as a basis for general conclusions, but it seems at any rate possible that the act of vomiting is under the same kind of control as defaecation and micturition, i.e. a fundamentally reflex mechanism vested in the organ itself and its own nervous connections, *assisted by* a strong increase of intra-abdominal pressure. The afferent impulses which normally initiate the act of vomiting are a result of the presence of substances in the stomach which threaten to damage its lining. They may also arise from touch receptors in the throat, from taste receptors in the tongue and from smell receptors in the nose. Fortunately many poisons taken in large doses cause vomiting and they may be eliminated before they can do any harm. The other side of the picture is that, if corrosive damage has already started, the increased pressure inside the stomach may rupture it at the weakened place. In giving emetics such as mustard, which though irritant is itself unlikely to do much damage, it is important to know something about the nature of the substance it is desired to expel.

Although vomiting is a comparatively rare act in the life of an ordinary individual, there is a definite centre in the medulla which controls the necessary reflexes. Curiously enough it may be thrown into activity by a drug, apomorphine, which in appropriate doses seems to have practically no other effect on the body.

CHAPTER XVIII

THE ENDOCRINE ORGANS

IN Chapter XV we made one or two references to "chemical messengers". These were quite early christened ***hormones***, a word derived from the Greek and having the same meaning. It now has a wider significance and is applied to many substances which circulate in the bloodstream. Some of these like gastrin, secretin, enterogastrone and cholecystokynin are produced by the cells of some part of the alimentary tract and after circulating in the bloodstream influence a related organ. Others are produced in special collections of cells which have no fundamental connection with organs in their vicinity, and belong to no system of the body we have so far considered. These collections of cells are called ***ductless*** or ***endocrine glands***, because they pour their secretion directly into the bloodstream and not into a duct. When we consider them in detail it will be seen that the description "chemical messengers" is appropriate for some of the secretions but not quite so appropriate for others. Many of them seem to have the same kind of function as the vitamins. That is to say, they are essential for the successful carrying out of certain cellular processes, and cells performing dissimilar functions may be equally dependent upon the presence of a certain hormone in the bloodstream. The ductless glands are (1) the anterior and posterior pituitary, (2) the thyroid, (3) the parathyroids, (4) the suprarenal cortex and the suprarenal medulla, (5) the ovaries and testes.

The order in which these have been placed is simply that in which they lie in the body starting from the head and working downwards. For our purpose it is convenient to treat them in another order and we will start with the suprarenal medulla.

The Suprarenal Medulla

The suprarenal glands are two relatively small yellow bodies near the kidneys (fig. 88). Microscopically the outside part of the gland (the cortex) is different from the centre part (the medulla) and so far as our knowledge goes at the moment, these two parts seem to be functionally independent. In other words, we are dealing with two ductless glands and not one.

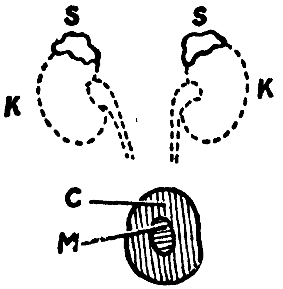


FIG. 88

The position of the suprarenals S, in relation to the kidneys, K. If the gland is sliced through the middle the difference in texture is seen between the cortex, C, and the medulla, M, of the gland.

The medulla of the suprarenal presents two striking features which help us to understand two of its functions. The cells of which it is composed have an unusual nerve supply. First, unlike those of any other abdominal organ they are supplied by nerve fibres whose parent nerve cells lie in the spinal cord. (Every other organ, with the exception of voluntary muscle, is supplied by fibres whose cell bodies lie in the peripheral ganglia of the sympathetic nervous system or in the corresponding relay stations of the parasympathetic. These outlying neurones are of course controlled by cells lying in the spinal cord, but the fact remains that the connection between the latter and the effector organ is indirect.) Secondly, although the cells of the suprarenal medulla are not shaped like nerve cells, they have an affinity for certain stains which are used for identifying nervous tissues. The inference is that the gland cells are in some way similar to the nerve cells of peripheral ganglia, although no nerve fibres spring from them.

When impulses pass down the nerve to the suprarenal and throw the cells of the medulla into activity, a number of events take place throughout the body which are identical with the effects of stimulating local sympathetic nerve supplies. This can be shown in anaesthetised animals by dissecting out the nerve to the suprarenal, applying electric shocks to it, and observing the effects of the stream of impulses so produced. Since the nerve goes only to the gland and the gland has no communication with other parts of the body except by the blood stream, it may be assumed that the effects are brought about by the secretion of some active substance into the generous network of capillaries with which the gland is supplied. This conclusion is confirmed by the fact that by collecting suprarenal glands from the slaughter-house and treating them with chemicals, a substance, *adrenaline*, can be extracted from them which, when injected into the blood stream, has all the effects of an electrical stimulus to the nerve supplying the gland.

Fairly recent researches have established the fact that nerve fibres arising from cells in sympathetic ganglia exert their effects by producing adrenaline or a substance almost indistinguishable from it at the junction of nerve fibre and effector cell. Let us take a specific example: when we say that nerve impulses pass down a fibre to the smooth muscle of an arteriole and cause it to contract, we mean that nerve impulses pass to the end of the fibre, where they liberate a minute quantity of adrenaline and this causes the muscle fibre to contract. So far as we know, exactly the same preliminary processes take place in the smooth muscle of the alimentary tract, except that the adrenaline liberated in or on these cells causes them to relax. The reason for this is not understood. Even all blood vessels do not react in the same way. For instance, the arterioles which carry the blood supply to heart muscle are dilated (i.e. the smooth muscle in them is relaxed) both by adrenaline injected into the circulation and by stimulation of the sympathetic nerve supply.

The experiments by which these facts have been found are too complicated to describe in detail, though the idea underlying them is fairly simple and well illustrated by the first experiments which led to the discovery. A frog was killed and its heart removed and attached to an apparatus (fig. 89) which allowed oxygenated salt solution to run through it. Since the frog is a cold-blooded animal its tissues use oxygen at a much slower rate than those of warm-blooded animals, and the heart muscle will remain alive and cause the heart to beat for hours and even days after it has been removed. Glucose can be added to the fluid to provide fuel, but the glycogen stored up in the muscle cells is sufficient to last for quite a long time. It was found if the nerves running to the heart were removed with it, that stimulating them with electric shocks had the same effect as in the body. If now the fluid which had passed through the heart was collected and passed through a second heart, on stimulating the nerve to the first heart, both hearts behaved similarly. If the first one speeded up, the second one did likewise. If the first one slowed down, the second one slowed down also. We are more concerned at the moment with the cause of the speeding up, but it is quite clear that in each case stimulating of the nerve released a chemical substance which acted on the muscle of the first heart, overflowed into the perfusing fluid and then exerted its effect on the second heart.

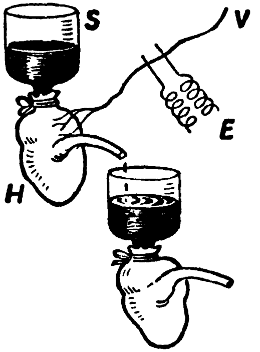


FIG. 89. The method for showing the influence of nerve impulses on the chemical composition of the fluid showing through an isolated frog's heart, and influencing a second heart.

H, excised frog's heart kept alive by passing oxygenated salt solution, S, through it. The latter is then allowed to run through a second heart. V, nerves to heart. E, wires for electrically stimulating the nerve.

It is not surprising, therefore, that the liberation of adrenaline into the blood stream has much the same effect in the body as would have a generalised stimulation of the sympathetic nervous system. There are one or two exceptions to this rather sweeping statement. For instance, the sweat glands which are supplied by the sympathetic nervous system do not respond to adrenaline, but to another chemical substance, acetylcholine, which happens to be liberated at their nerve endings. This is an important fact to bear in mind, but possibly more important is the fact that the action of adrenaline on an isolated organ is not always faithfully reproduced when adrenaline is injected into the bloodstream.

With a few more precautions as to temperature and oxygenation, the heart of a rabbit can be caused to beat outside the body in much the same way as the heart of a frog, and the application of adrenaline to such a preparation will cause the frequency of the heart beat to increase. When adrenaline is injected into the blood stream of the intact animal it sometimes makes the heart beat faster, but often more slowly. The reason is not any difference in the relationship between adrenaline and cardiac muscle, but that the vagus (parasympathetic) nerve to the heart has been reflexly activated to exert an opposite and overriding influence. The afferent impulses of this reflex originate in the stretch receptors of the aorta and carotid artery (see page 120). The stretching has been brought about by a rise of blood pressure caused by the powerful constricting action of adrenaline on the arterioles. Cutting the vagus nerve, which is the efferent path of the compensatory reflex, allows the heart to respond to the adrenaline and its rate then increases enormously. The arterial blood pressure may rise to more than double its normal value.

We are less familiar with the background against which some of the other hormones work, but this example shows how dangerous it is to jump to conclusions about the action of a hormone in the body purely on the basis of its action on individual organs. It is important to know what the latter action is, and in most cases it runs true to form in the intact animal, but the body is more than a collection of isolated organs and, when its integrity is threatened by independent action on their part, compensatory reactions are thrown in.

Noteworthy instances of the action of adrenaline on various parts of the body are as follows:

The hairs of the scalp and elsewhere are erected by means of the small muscles attached to them (see page 35).

The pupil of the eye is dilated. (The black part of the pupil is really a hole in a circular curtain through which the light passes, and the curtain contains muscle fibres which run either in a circular direction or radially. The latter are supplied by sympathetic nerves controlled by cells in the spinal cord, and adrenaline makes them contract, thus widening the aperture.)

The small bronchi which have smooth muscle running round them (see page 146) are dilated by adrenaline (and by excitation of their own sympathetic nerves) so that air flows more easily in and out of the lungs. This property of adrenaline is extensively used in the disease of asthma, in which the bronchial muscles are spasmodically contracted.

The heart is accelerated and its beat made more forcible.

The muscle of the alimentary tract is in general relaxed, although in those places where rings of muscle are used to hold back the food it may be contracted. The whole effect is to delay the passage of food through the gut and is again the same as that of the sympathetic nervous system.

The cells of the liver are caused to break down some of their glycogen and transform it into glucose, which is passed into the blood stream, and injection of adrenaline may, therefore, cause a rise in the concentration of sugar in the blood.

The urinary bladder tends to be relaxed by adrenaline and by the sympathetic nervous system, but their actions do not seem to be very important, since the bladder will empty fairly normally and remain under control when the sympathetic nerve supply has been removed (the parasympathetic supply from the sacral part of the cord must, however, be intact).

The arterioles and capillaries of the skin and abdominal viscera are constricted, those of the heart are dilated and those of the brain and lungs are very little affected. There is some doubt about whether the blood vessels of voluntary muscle are actively dilated by adrenaline or whether the absence of a constricting action allows them to be dilated by other agencies (see page 126).

Most of these individual effects can be demonstrated by administering extremely small doses of adrenaline, and the question naturally arises whether the suprarenal glands are all the time contributing a certain amount of adrenaline to the blood stream, or whether it is discharged by them only at certain times. There are various experiments which lead us to suppose that very small quantities are continually secreted, but there is no doubt that stimuli giving rise to fear, anger or other emotions cause a suddenly increased output. This is presumably due to a burst of nerve impulses which have their origin in the general pattern of central nervous activity induced by the emotion, and which reach the gland in the nerves supplying the suprarenal. It is clear that the general vasoconstriction (shown by pallor of the skin), the rise of blood pressure, the discharge of glucose into the blood stream, the inactivation of the alimentary tract and the increased diameter of the bronchi are excellent preparation for sudden muscular activity which, in the shape of " fight or flight " would be the normal automatic response. It is not very clear how far the emotional feeling associated with fear, anger, etc., is due to the physical changes associated with it and how far it is the conscious component of the nervous activity which precedes the physical changes.

The medulla of the suprarenal probably acts as a reinforcement to the sympathetic nervous system, and it is not essential to life. Animals can live without it. This, however, is probably because the sympathetic nervous system at all its nerve endings is producing adrenaline or something indistinguishable from it, so that although the animal is deprived of the gland it is not altogether deprived of the type of activity which the gland represents. If both the suprarenals and the sympathetic ganglia are removed from an animal, a feat of surgery which has been successfully carried out in America, cats are able to live apparently quite happily so long as they are not exposed to physiological emergencies such as extremes of temperature, or the necessity for hard muscular work. In one sense, therefore, adrenaline is not essential to life, but in an animal unprotected from its environment, it is essential.

The Suprarenal Cortex

Unlike the medulla, the cortex or outside part of the suprarenal is absolutely necessary for life. If it is removed in animals or destroyed in man by disease, as sometimes happens, the individual dies. The obvious symptoms are muscular weakness, loss of appetite, a fall in body temperature and a reduction in the arterial blood-pressure. A chemical extract of the suprarenal cortex contains something which will counteract these effects both in animals and in man, though in the case of the latter the disease which has attacked the suprarenal may become fatal by spreading to other parts of the body. Just what the substance or substances are which the suprarenal cortex contributes to the blood stream is a matter for speculation. A large number of closely related chemical bodies known as steroids have been isolated from it and all of them cause some alleviation of the symptoms of deficiency and prolong life. Some of their actions are quite remarkable, but there are good reasons for believing that the final answer to the problem of suprarenal cortical activity has not been found. The isolation of numbers of pure steroids from suprarenal tissue is no proof that they are all being continuously manufactured and passed into the blood stream, although this is quite possible. The secretion of a certain combination of them might account satisfactorily for the action of the cortex, but as its absence is better compensated by a "total" extract than by any one of the steroids individually; the solution of the puzzle may lie with some substance as yet undiscovered. The fraction of an extract which is left after all the chemically identified substances have been removed is certainly very active.

Underlying the symptoms of suprarenal deficiency is a maldistribution of salts and water in the body, a sluggishness in the conversion of amino-acids to carbohydrate, and other disturbances more particularly associated with the loss of muscular power. There is a great excretion of sodium chloride (common salt) and the addition of large quantities of this substance to the diet is very beneficial, allowing much smaller doses of cortical extract to be used for the purpose of maintaining life.

Over-activity. In children and women there is sometimes an overgrowth of suprarenal cortical tissue and this has surprising effects which appear to bear no relation to those we have described as resulting from deficiency. They consist in boys of precocious maturity, while in girls and women changes such as the growth of hair on the face occur which are usually associated with the male sex. The ovaries and testes also produce steroids not very different chemically from those made by the suprarenal, though the physiological influences which they exert are very different. The most likely explanation of the effect of over-active suprarenal cortical tissue is that its activity is not only increased, but changed in some way so as to produce the wrong kind of steroid.

In discussing this gland we have plunged into a sea of uncertainty, in which the hormones with which we are concerned are much less simple in their action than those of the alimentary tract. The secretion of the suprarenal medulla, adrenaline, was also complicated in its effects, but it had the merit of being a fairly simple substance, fully adequate to account for all the observed activities of the gland from which it originated. The idea of a relatively small piece of tissue represented by the suprarenal cortex producing a number of fairly complicated substances, none of whose effects is able completely to account for the activity of the gland, and yet none of which could be at this stage in our knowledge excluded from its activities, is new. The problem is made more difficult by the fact that these substances act on processes which are not easy to isolate and study by themselves. The distribution of sodium and the control of the supply of carbohydrate are things which involve the whole body. The reason why the actions of adrenaline have been well worked out is that they are exerted so frequently on cardiac or involuntary muscle, which is easy to keep alive outside the body. When all parts are exposed simultaneously to adrenaline, it may perhaps be a little difficult to work out the resultant effect, but at all events we have a good idea of the elements with which we are dealing. In the case of the suprarenal cortex we await the arrangement of the many facts which have been discovered into a well-understood scientific pattern.

The Thyroid Gland

The thyroid gland lies buried in the soft structures of the neck and its two main lobes are joined by a band of thyroid tissue which runs across the front of the windpipe. We can, therefore, speak of it as a single organ. Its microscopic structure is shown in fig. 90*b* and although it has a very copious blood supply it will be seen that the secreting cells line fairly considerable cavities in which a jelly-like material is stored. This is thought to contain the active principle of the gland, but instead of being stored within the cells like glycogen is in the liver, it is kept in these much larger depots. Experience has proved that when a gland is relatively inactive the store of colloid material becomes very large and this may in turn cause an enlargement of the whole gland. When the gland is very active the hollow vesicles tend to be small, but they may also be numerous and again lead to a general enlargement of the gland.

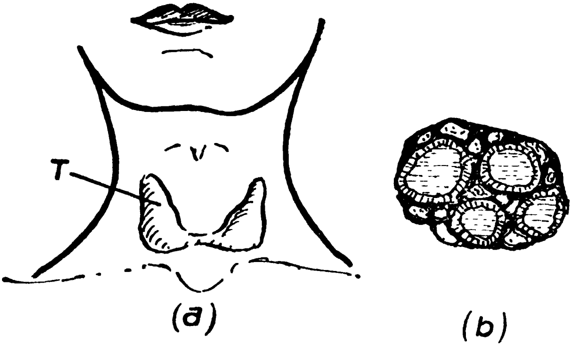
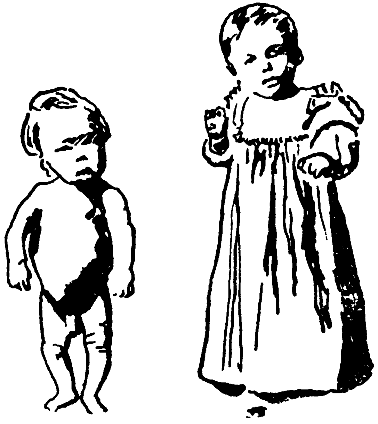


FIG. 90

(a) To show the position of the thyroid gland, T, in the neck. (b) Microscopic structure of gland. The horizontally shaded areas indicate the colloid surrounded by the cells which have produced it. In between the vesicles run numerous capillaries (stippled).

The active principle of the thyroid gland is called *thyroxin*, a chemical substance which is much simpler than the steroids which are produced by the suprarenal cortex. It is rather more complicated than the adrenaline of the suprarenal medulla. There is some evidence to suggest that thyroxin itself may be part of a much bigger molecule which the cells of the thyroid manufacture, but if so it is undoubtedly the significant part of the molecule and the remainder does not matter very much. The fact that we have a simple substance to deal with, and that the symptoms of over-activity and under-activity are often associated with a tell-tale enlargement of the thyroid gland, makes the problem of elucidating its function much simpler than that of the suprarenal cortex. On the other hand, we cannot pick out any particular place or places in the body on which thyroxin acts. It has a very deep-seated action which permeates the whole body and is manifested in two chief ways.

(*a*) In the fully formed individual it determines the basal metabolic rate, that is to say, the fundamental rate at which the tissues use oxygen. Thus, persons in which it is lacking are mentally sluggish, physically inert and have a low metabolic rate, while those in whom its action is excessive are mentally alert to the point of distraction, physically restless (though probably incapable of prolonged exertion) and have a high metabolic rate.



(*a*) (*b*)

FIG. 91.

(*a*) Cretin, 23 months old, before treatment. (*b*) The same child, 34 months old, after 11 months' administration of sheep thyroid. (Sketched from photographs by Osler.)

(*b*) In the growing individual it determines the process of development. A baby suffering from thyroid deficiency fails to grow either mentally or physically, but the physical stunting is not uniform and the various deformities associated with *cretinism* occur. Such children may live to an adult age, but their mentality remains that of a child of 3 and they are at the best grotesque caricatures of human beings.

These two principal activities are undoubtedly inter-related, but to what degree it is difficult to say. In adults suffering from thyroid deficiency structural changes occur, some of which are also seen in cretins, though of course as the body is already fully formed, the major deformities of cretinism cannot occur. Conversely, in cretins the basal metabolic rate is low, but we are not in a position to say that the general under-activity of the tissues of the body is the cause of their failure to develop normally.

The most striking thing about *thyroid deficiency* is that it can be completely alleviated by administering dried thyroid gland or thyroxin itself. This does not restore the power of the thyroid itself to produce thyroxin and if the treatment is not maintained the patient relapses. The pictures in figs. 91*a* and 91*b* are sufficiently graphic to indicate the remarkable effects of thyroid replacement.

Research has, however, gone even further than this. The most important constituent of the molecule of thyroxin is the substance iodine, and in districts where this is deficient in the soil and therefore in the diet, widespread thyroid deficiency may occur. Individuals are affected to different degrees, some showing frank signs of thyroid deficiency while others are quite normal. An intermediate group may be normal in nearly every way except that they show an enlargement of the thyroid gland which may be considerable and itself constitute a major deformity. Cretinism also tends to occur in these districts and is almost certainly due to the mother's lack of iodine. The introduction of small amounts of compounds of iodine into the salt used by the inhabitants of the region or added to the diet in some other way has effected an enormous reduction in the incidence of thyroid deficiency (fig. 92).

Until recently no such simple way of treating *over-activity* of the thyroid has been available, and recourse has been had to removing a large part of the gland. There is no suggestion that excess of iodine in the diet has anything to do with over-activity of the thyroid, though it uses iodine at an increased rate.

This means that the supply of iodine is likely to be insufficient for it and to this extent it resembles the gland of an individual who is suffering from a genuine deficiency of iodine. The natural

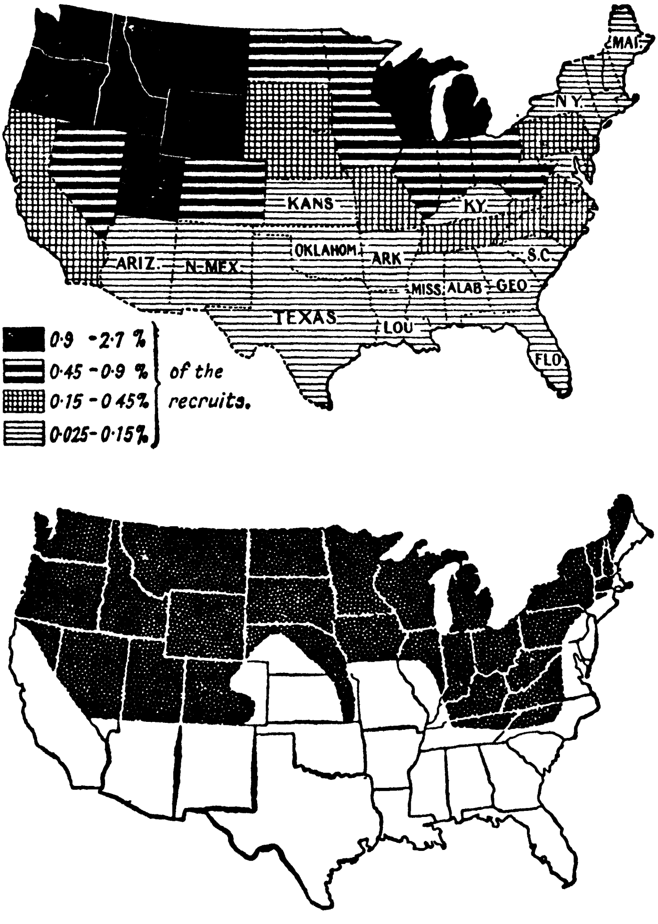


Fig. 92. Comparison of iodine in water supplies (bottom) with distribution of goitre (top).

Stippled part of lower map: less than 0.2 parts of iodine per billion parts of water.

response to lack of iodine either absolute or relative seems to be for the gland to increase in size as though by doing so it could produce more thyroxin. Some of the microscopic appearances of the over-active and under-active gland may, therefore, be similar, but in the former the signs of activity—small and numerous vesicles—are obvious and the enlargement never proceeds to the same length as it may do in the latter.

The explanation of over-activity, in so far as it can be called an explanation, seems to be that the activity of the gland is " set " at a higher level and we do not know how the setting is controlled. Both the nerves supplying the gland and another hormone (the thyrotropic hormone) secreted by the anterior pituitary are able to increase its activity, but there is no good evidence that either of these agents is at fault in a thyroid gland which is over-active. Cutting the nerves has proved ineffective as a cure and the administration of thyrotropic hormone to animals does not seem to have the lasting effect characteristic of the condition found in human beings. A new drug (thiourea), discovered recently, which promises to alleviate the symptoms of over-activity of the thyroid does not subdue the effect of artificially administered thyroid, and the inference is that it interrupts the formation of thyroxin by the gland. Although likely to be of great importance this throws little light on the fundamental disturbance responsible for the condition.

The Posterior Pituitary Gland

The pituitary like the suprarenal is a double gland. The posterior part is developed originally from an outgrowth of the brain and the anterior part from an outgrowth from the roof of the mouth. The two pieces of tissue with these diverse histories are very closely associated and lie in a bony hollow at the base of the skull (figs. 70 and 93). The anterior part of the gland has a cleft in it and it is the portion in front of this cleft which is usually known as the anterior *lobe* of the gland. The part behind the cleft is firmly attached to the posterior part and adheres to it when the gland is split. It therefore forms part of the posterior lobe. It is very difficult to say how far the developmental history of these parts of the gland is important. For the purpose of making chemical extracts and investigating the function of the gland, we simply take things as we find them and use the anterior lobe and the posterior lobe, bearing in mind that the latter really consists of a " pars intermedia " and " pars nervosa ". The last is still connected to the brain by a stalk containing important nerve fibres. The anterior pituitary is perhaps the most important of the ductless glands, but we shall not consider it at this point (see page 239).

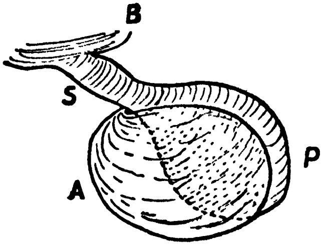


FIG. 93. The pituitary gland showing its different parts.

A, anterior, P, posterior lobe. S, stalk. B, brain. The stalk is attached to the base of the brain and the position of the gland in the skull is indicated in Fig. 70.

Now the fact that a substance which has a profound action on the body can be extracted from a tissue by chemical means is no proof that the tissue habitually contributes this substance to the blood stream. Many substances can be obtained from all kinds of living tissue and, so far as we know, they are of limited physiological importance. Confirmatory evidence is needed to establish that a substance is significant. Adrenaline, extracted from the suprarenal medulla, can be demonstrated in the blood leaving the suprarenal gland on stimulation of its nerve supply, and the actions of the naturally occurring substance are identical with those of the extract. Whatever may be our doubts about the actual substance produced by the suprarenal cortex, we are aware that when the cortex is absent or diseased that there is a deficiency in the body which can be remedied by administering chemical extracts of the gland. The extracts are therefore definitely related to the known function of the gland. The significance of thyroxin is again quite clear. Over-activity of the gland corresponds very closely with the effect of administering too much thyroxin and under-activity of the gland can be corrected by it.

Matters are not so simple in the case of the posterior pituitary gland. Extracts, made in a certain way, have a profound action on the muscle of the uterus, which is thrown into strong contraction, and the extract is an important weapon in the armoury of the obstetrician. Nevertheless, evidence that such a substance plays any part in the strong contractions of the uterus which occur during and after birth is scanty, and indeed some animals are known to be capable of giving birth to their young in the absence of the posterior pituitary gland. There is a certain amount of evidence that such a substance can be liberated into the blood stream by electrical stimulation of the gland, but its function is not yet clear.

Extracts made in another way will act on smooth muscle in other organs, particularly the arterioles. It is again doubtful whether this action has great physiological significance, for the arteries of the heart share in the constriction. This means that at the same time as the heart's action is made more difficult by a rise in the pressure against which it must beat, its own blood supply is impaired by vasoconstriction. However, the fact that we are able to visualise very few, if any, situations in which such an action would be advantageous is no proof that it does not occur, and we must await further evidence. This "pressor" principle (so called because of its effect on blood pressure) is now known to have a marked effect on the kidneys in concentrations much smaller than those which affect the blood vessels, and this may indicate its true function: *it is always dangerous to assume that the physiological adjective applied to a newly discovered active principle represents its real action.*

When a large drink of water is taken we have seen that the additional fluid is very quickly eliminated by the kidneys by means of a copious flow of urine. The temporarily large flow of urine is called a diuresis, and as there are many other ways of increasing the flow of urine the type we have just described is called a *water* diuresis. An extremely small quantity of the pressor pituitary extract will bring a water diuresis to an abrupt close, similar to the sudden interruption of flow which occurs if the individual begins heavy work or receives sudden painful or other stimuli. Although the kidney can eliminate excess water in the absence of the pituitary gland it will not do so quite so neatly, and most experts believe that posterior pituitary secretion is normally present in the bloodstream and that it helps to control the amount of water reabsorbed by the tubules of the kidney. This point of view is reinforced by our knowledge of a distressing disease known as diabetes insipidus, which occurs in persons whose posterior pituitary gland is damaged or severed from its connection with the brain. These people may be regarded as in a continual state of water diuresis, in which they excrete large quantities of water which has to be restored to the body by drinking. Just as posterior pituitary extract will stop a water diuresis, so it will check diabetes insipidus. The importance of posterior pituitary extracts, therefore, lies in their uterine or " oxytocic " action and in their anti-diuretic effect. There is more evidence that the latter represents a normal function of the gland than that the former does.

CHAPTER XIX

THE ENDOCRINE ORGANS (*continued*)

The Pancreas and Insulin

We have already seen that the suprarenal and pituitary each comprise two ductless glands. It need not surprise us, therefore, that scattered about in the pancreas, which pours a very important digestive juice into the duodenum (p. 192) there are islands of cells which have nothing whatever to do with this function and which have no connection with the alimentary tract. They pour their secretion directly into the bloodstream, and are known as the *islets of Langerhans*. We do not know why they are arranged in this particular way and why they are not collected in some part of the body to form a separate organ like the suprarenal, thyroid or pituitary. It is very well known that the active substance which they contribute to the body is *insulin* and that it has an important effect on the metabolism of carbohydrates.

On page 198 we described how the level of sugar in the blood was maintained by the liver, and at first sight it may seem that nothing further is necessary for the correct utilisation of carbohydrate food. However, we omitted one important qualification, namely, that the liver is unable to carry out this particular function without the assistance of substances circulating in the bloodstream. There are several of these, influencing in various ways the performance of the liver, whose ability to respond correctly to the needs of the organism depends on there being a proper balance between them. One of the most important is insulin, and the consequences of its absence or deficiency are very well seen in the disease of diabetes mellitus. As in diabetes insipidus there is a copious flow of urine, but this time the significant substance which is responsible is glucose.

The immediate reason for the appearance in the urine of this abnormal constituent is that there is a greater concentration of it than usual in the blood and therefore in the glomerular filtrate of the kidney. The tubules presented with this abnormal amount are incapable of reabsorbing all of it. The normal concentration of glucose in the blood is about 100 mg. in 100 cc. If this rises moderately, the kidney can still deal with it by returning all which appears in the glomerular filtrate to the blood. But when the blood sugar concentration reaches about 180 mg. per 100 cc., sugar begins to appear in the urine.

In the absence of insulin, levels of blood sugar much greater than 180 mg. per 100 cc. are encountered and a great wastage of glucose ensues. The liver is not doing its job properly, and, in fact, it is behaving in what appears to be a completely uncontrolled fashion. Even if by dieting it is deprived of the supply of sugar which it gets from the alimentary tract, it will continue to manufacture an abnormally large amount from protein (see p. 200) and pass this into the blood stream.

In addition to this disturbance of the liver it has been found that the muscles fail to make full use of the sugar in the blood stream, so that not only are the tissues being presented with an unusually large quantity of glucose, but they fail to utilise even as much as usual. It is unnecessary to go into further technical details to show what a serious state of affairs this is. The body is largely thrown on its resources of protein and fat, and is faced with the further difficulty that when glucose is being insufficiently utilised the oxidation of fats becomes upset. This may be due to a close dependance of fat upon carbohydrate metabolism, or to an increased call upon fat to supply the deficiency of fuel and an overloading of the chemical mechanism responsible for its oxidation. When this is incomplete certain acid breakdown products of fat are released, with a resulting threat to the stability of the hydrogen ion concentration of the blood.

The brilliant researches which led to the isolation of insulin, and the dramatic effect its commercial production has had on the prolongation of life in diabetics, have resulted in a widespread knowledge of its importance. Since then it has been found that other endocrines play a part, and perhaps as important a part as insulin. The methods of investigation used have been the removal of various glands and the administration of extracts made from them. It is often necessary to experiment in this way with two glands simultaneously and, as excess or deficiency of a particular secretion may have other effects besides those on carbohydrate metabolism, the results are not always easy to interpret. It is apparent, however, that the *anterior pituitary* gland and the *suprarenal cortex* each exert an influence on the liver which is roughly the opposite of that of insulin.

This aspect of the subject is further complicated by the fact that the anterior pituitary gland also contributes a substance to the blood without which the suprarenal cortex cannot live. In an animal whose anterior pituitary has been removed, the suprarenal cortex diminishes greatly in size and almost disappears.

Adrenaline, the secretion of the medulla of the suprarenal, is also important in carbohydrate metabolism because it stimulates the liver to break down its glycogen stores and turn them into glucose; a sudden discharge of glucose into the bloodstream from this cause can be of great value. *Thyroxin* tends to exert a more prolonged effect of the same kind, keeping the blood sugar on the high side and the glycogen stores of the liver very mobile. This correlates very well with its general action on tissues, of stimulating their rate of oxidation. The effective utilisation of carbohydrate depends therefore on the balanced action, much of which is exerted on the liver, of the secretions of several ductless glands, and there is also evidence to suggest that a nervous centre in the hypothalamus may play a part.

We have progressed a long way from the relatively simple " chemical messenger " type of action of gastrin and secretin, and there is no doubt that the exact mixture of very potent chemical agents circulating in the blood exerts a control over the chemical processes of the body which is second only in importance to the more immediate and obvious kind of control exerted by the nervous system.

The Parathyroid Glands

These glands, as their name suggests, lie very close to the thyroid. They are four in number and are quite small in size, not much larger than peas, and sometimes difficult to find. The effect of their internal secretion is upon the exchanges of calcium and phosphorus in the body, and they must work together with vitamin D in some such way as those hormones work together which influence the exchanges of carbohydrate. The details of the way in which the parathyroids act are not fully understood, but we do know that the amount of calcium in the blood (normally about 10 mg. per 100 cc.) falls if the parathyroids are removed or not functioning properly.

A correct concentration of calcium in the environment of nerve and muscle is essential for their proper activity, and a fall in the calcium content of the blood leads to the disease of *tetany*, in which the muscles go into uncontrollable contraction and the individual suffers from convulsions. This condition can be relieved by administration of an extract of the parathyroid glands and temporarily alleviated by injecting salts of calcium into the bloodstream. If quantities of the active extract *parathormone* are administered to an individual who is not suffering from parathyroid deficiency, then the concentration of calcium in the blood rises and leads to various symptoms which we need not describe. The chief point to be noted is that the additional blood calcium has to be obtained from somewhere, and it actually comes from the most plentiful store of calcium in the body, namely, the bones. They may then become soft, and bend or break.

The behaviour of calcium in the body is complicated and intimately bound up with that of phosphorus. Its compounds tend to be insoluble in water, and the solubility of those which it forms with phosphate is greatly influenced by the hydrogen ion concentration of their surroundings. So for as excitable tissues like nerve and muscle are concerned it is important that calcium should be present in solution, but so far as the bones are concerned it is important that the calcium salts deposited there should not be too easily washed out by the blood flowing through them. The presence of calcium is also essential in many chemical processes in the body, such as the clotting of blood.

Parathormone and vitamin D between them control in some way the type of substance with which calcium is combined, so that it may be got in and out of the body. Thus provision has to be made for its absorption in the small intestine and its excretion in the large intestine and to some extent in the urine, and a proper equilibrium has to be maintained in the neighbourhood of bones. Just how this is effected we cannot say, but the malformation of growing bones which can appear in rickets, the softening of bone which can occur in pregnancy through lack of calcium in the diet, the softening which can result from over-activity of the parathyroids, the formation of deposits giving rise to stones in the urinary tract and the gall bladder, and the occasional calcification of soft tissues, are a sufficient indication of the importance of the equilibrium.

The Anterior Lobe of the Pituitary

We have left this gland until the last because it is thought to have an influence on nearly all the others, and it is possible that one of the most important functions of its secretion is to set and maintain the balance of hormones in the body. Thus, operative removal of the anterior pituitary gland from an animal results in a shrinkage (*atrophy*) of the thyroid, the parathyroids, the suprarenal cortex, the islets of Langerhans, the ovaries and the testes. We shall see that the last two have a definite chemical activity besides their function of producing ova and spermatazoa and are true ductless glands. An extract of the anterior pituitary gland which will maintain these other glands is fairly easy to prepare, but it is remarkable that further treatment of such an extract has been successful in separating from it fractions which will, for instance, maintain the thyroid gland and not the others, the suprarenal cortex and not the others and so forth. In other words, there is evidence that the anterior pituitary produces not one substance which enables the remaining ductless glands to live and function, but several substances; hence the possibility that it can control their activities selectively and balance one against the other. The investigation of this side of the activity of the anterior pituitary is yet in its infancy, but there is already abundant evidence that it produces two substances which play upon the ovary, rhythmically modifying its activity. If it does the same sort of thing in relation to the other ductless glands, then its function must be very complicated and very important indeed.

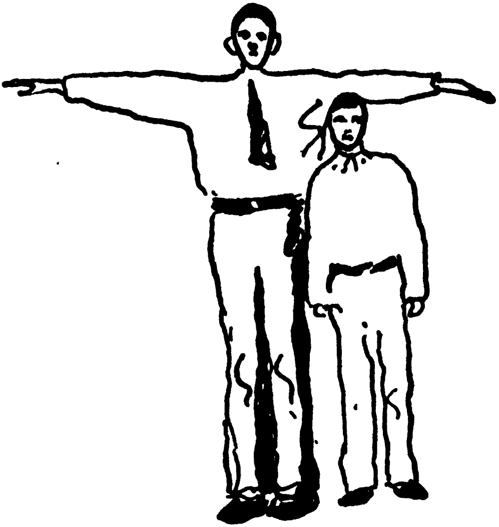


FIG. 94. A pituitary giant (aged 13½) compared with a normal man (his father) as sketched from a photograph by Behiems & Barr (*Endocrinology*, 1932).

The anterior pituitary has, however, certain properties which it appears to exert directly upon the other tissues of the body. For instance, young animals from whom it is removed promptly cease to grow and it is taken for granted that the various types of human dwarf result from its deficiency. Sometimes it is over-active and giants are produced (fig. 94). It is interesting to note that these abnormalities are often accompanied by others which are obviously related to collateral functions of the gland. For instance, dwarfs are very often sexually immature and giants often suffer from a kind of diabetes (see p. 237). So far as we can tell, we must allow at present for the production by the pituitary of a special *growth hormone.*

Another important substance secreted by the pituitary is the *lactogenic hormone* which controls the production of milk in the breasts (*mammary glands*) and is therefore of great importance in the nutrition of the newly born infant. There is also a possibility that the pituitary is concerned in the *growth* of the breasts as well as with the actual rate of milk production.

The hormones which influence the growth and maintenance of various organs are distinguished by the suffix " trophic " or " tropic ". There is evidence, therefore, that the anterior pituitary produces the following hormones:

(1) thyrotrophic;
(2) adrenotrophic;
(3) pancreatrophic;
(4) parathyrotrophic;
(5) gonadotrophic (maintaining the ovaries and testes);
(6) mammotrophic (maintaining the mammary glands);
(7) growth hormone;
(8) metabolism hormone influencing carbohyrate metabolism, sometimes called diabetogenic;
(9) lactogenic.

For such a small gland this is a remarkable list, yet it does not include all the possibilities that have been raised. None of the substances mentioned has been obtained quite pure and in no case has the chemical constitution been defined. They all seem to be very complicated chemically and, in fact, are probably proteins. One must always bear in mind the possibility that in the process of extraction a very complicated substance may, as it were, have bits chipped off from its molecule and its properties thereby changed. The properties of the residual fraction might be different according to the portion of the original molecule which is lost. When we know more about the gland it may be possible to account for its effects on the basis of a smaller number of substances than that which it is now supposed to pour into the blood stream.

It is surprising that in spite of this very widespread activity, animals whose pituitaries have been removed do not immediately die, though they succumb more easily than normal animals to an unfavourable environment. Bearing in mind the disastrous results which ensue when some of the other ductless glands are removed, for instance, the suprarenal cortex and the parathyroids, we must assume that they are able to function to some extent in the absence of the anterior pituitary and our supposition that the latter may act as a controller and regulator is strengthened.

CHAPTER XX

REPRODUCTION

It is impossible to discuss all aspects of growth and reproduction in an introductory account, because these two subjects present some of the most fundamental problems of biology. We have already remarked that the shape of a fully grown bone is very much the same as that of the immature bone, yet the former can contain none of the original substance of the latter. Growth is obviously more than mere accretion, and involves a persistence of form which is difficult to account for. The development of a complete individual from a single cell is even more remarkable, if this is not too mild an adjective to apply. A hen's egg at first represents one cell together with a quantity of nutritive material. This cell multiplies by growing and dividing till millions of cells are produced and in the process the nutritive material of the egg is used up. But the actual development of these millions of cells into a chicken involves processes of differentiation of form and function which are not understood, though they can be followed step by step. Fig. 95 shows a succession of such steps obtained by examining microscopically various stages between the single cell and the completely formed individual.

If the bud of a limb is taken (long before the limb is fully formed) and cultured outside the body, it can be kept alive sufficiently long for a certain amount of growth and development to take place. That part of it which would have been destined to be bone grows according to a shape which is quite recognisable as that of the mature bone in question. To some extent, therefore, the formative factors are inherent in the particular cells we started with. If, however, we pause and think backwards into the history of these cells, we come finally to the original cell from which they, in common with every other cell of the body, started, and it is clear that the tendency to develop into a leg or an arm has been acquired at some stage in the process of multiplication.

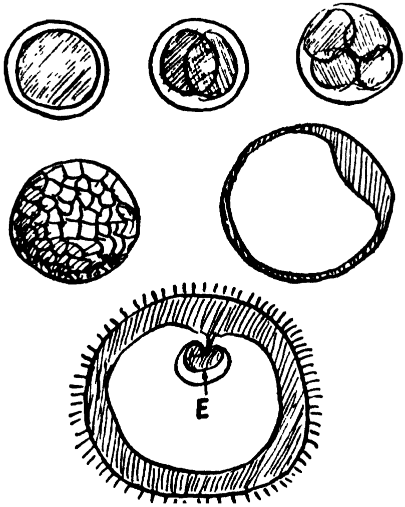


FIG. 95. Stages in the division of an egg to form increasing numbers of cells which gradually arrange themselves to form the parts of the future individual, E.

No regard is paid to magnification. The *villi* in the last sketch which attach the embryo to the mother later disappear from all parts of the surface except that underlying the foetus E. This part is then known as the placenta (Fig. 101).

The individual in the making is known as the *embryo* and a vast amount of research has been carried out on the embryos of animals which develop outside the body of the mother, e.g. those of reptiles and birds. Many of the factors determining the course of development have been discovered and chemical substances known as " organisers ", whose name describes their function, have been found. But these must also have been made during the course of development from a single cell. We cannot get much beyond the fact that an egg has the inherent power of developing into an individual similar to that from which it is derived, a fact which holds good throughout the plant and animal kingdom.

In the mammals, which comprise most of the warm-blooded animals we meet with on land, the development of the egg takes place inside the mother's body instead of outside. It is only to be expected that the developing warm-blooded animal must be kept in a warm environment, and this is the best way of doing it. Instead of having to rely on a supply of food and raw materials deposited with it (as in the egg of the bird), it is able to obtain these from the blood stream of the mother as it wants them. Mammalian eggs are, therefore, quite small and contain just sufficient protoplasm to tide them over the short period between leaving the *ovary*, where they are formed in large numbers, and becoming embedded in the *uterus* which is the organ in which they develop (fig. 96). Once in the uterus, into the lining of which they sink, they obtain nourishment from the tissue fluid with which they are surrounded until their development has gone so far that the embryo has a circulatory system of its own. This circulatory system then comes into close relationship with that of the mother, and although the bloods do not mix they are separated only by thin layers of cells which allow nutritive materials, oxygen, carbon dioxide, etc., to pass across from the side in which they are more concentrated to that in which they are less concentrated.

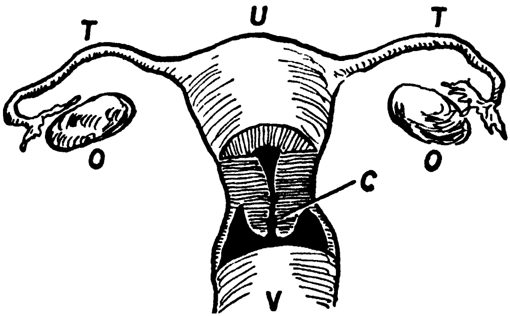


FIG 96. Female reproductive organs.

O, ovaries. T, uterine tubes. U, uterus, partly cut open to show the cervix, C. V, vagina.

The human embryo remains in the uterus for forty weeks, by which time it has achieved the weight of about seven pounds, approximately 1/20th of the mother's weight. In three weeks a mouse, weighing say 30 grammes, may produce as many as ten small mice each weighing 1 gramme, i.e. about 1/3rd of the maternal weight. Animals vary a great deal in the weight and degree of development of their young when these are born, but whatever these may be it is obvious that the process of *gestation* must require many adjustments in the physiological processes of the mother.

The maternal mechanism

The *primary sex organ* of the female is the ovary, a solid lump of tissue under the surface of which are thousands of cells which can develop into eggs. The sign that an egg is so developing is that the principal cell enlarges and becomes enclosed in a sphere hollowed out in the ovary and filled with fluid. The egg does not float free in the fluid, but is supported by a hillock of cells (the *cumulus*) whose base rests on the inside of the wall. The whole thing is called a "follicle" (fig. 97). The egg continues to grow and the follicle to swell, but if the animal is immature, the egg eventually dies, and the follicle subsides and disappears. If the animal is mature, the follicle continues to swell until it bursts and liberates the egg or *ovum*. The latter is picked up by the end of the *uterine tube*, in which it meets the germinal cells of the male. These are normally deposited in the female genital tract by the male himself, but in domestic animals they may be placed there by human agency. This is known as "artificial insemination", a process of increasing importance in animal breeding.

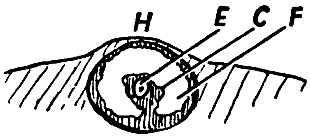


FIG. 97. Ripening follicle in ovary.

F, fluid. C, cumulus. E, egg. H, projection on surface of ovary.

The male germ cell, or *spermatozoön*, has very little protoplasm and this is in the shape of a threadlike tail which, by a kind of whipping movement, drives the cell forward. The spermatozoön is very much smaller than the ovum, the wall of which it penetrates. So far as nuclear material is concerned—and it is in the nucleus that the hereditary characters of the individual are carried—the contribution is equal, but so far as ordinary general cellular protoplasm is concerned, this is almost entirely provided by the female, so that the spermatozoön appears to be absorbed by the ovum. The nuclear material joins up, forming a single cell with twice as much nucleus as the ovum had before[1]. This single cell divides in the way we have indicated and ultimately forms the new individual, the material for growth being obtained from the mother.

Leaving the egg to its own devices and returning to the ovary, we find that in the place from which the egg came the cells which previously formed the cumulus, some of which were left behind, have themselves multiplied so as to fill up the cavity and have changed their character somewhat. They are now yellow in colour and closely packed, so that where once we had an egg follicle we now have a lump of yellow tissue known as a *corpus luteum* (fig. 98). After a while the cells of the corpus luteum lose their yellow pigment, shrink and cease to be of any account. While they are in their mature form, however, they perform an important function which we can best understand by turning now to the *accessory sex organs* (fig. 96).

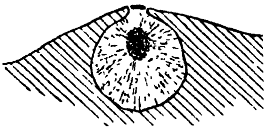


FIG. 98. Corpus luteum. Compare with Fig. 97.

The accessory organ which is at first of most importance is the *uterus*, a cavity lined by a moist membrane which is pitted with simple glands and invested by a thick sheath of muscle. This hollow organ has three small openings, two at the top leading into the *uterine tubes*, which represent the path taken by the egg in coming from one or other ovary on its way to the uterine cavity, and the third at the lower end. This last is also very narrow and rather long, and opens into the *vagina*, which communicates directly with the exterior, and in which the spermatozoa of the male are deposited. It is just as important that bacteria should be excluded from the uterus as that spermatozoa should enter, therefore it is thought that the entrance to the uterus—the *cervix*—is usually closed by the strong sheath of muscle which surrounds it. During the development of the embryo it is also generally plugged by a sticky secretion. The reader will appreciate that the cervix of the uterus is a very versatile organ, for while during the greater part of life its function is to exclude things from the uterus, and while this is not particularly incompatible with periodically admitting spermatozoa which are of microscopic size, when the young are born it has to dilate rapidly to a sufficient degree to admit of their expulsion from the uterus. In human beings this means achieving a diameter of about 3¾ inches.

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[1] As the normal amount of nuclear material has been halved during the original formation of ova and spermatozoa, the fusion which occurs on fertilisation produces a nucleus with once more the normal amount.

From the figures mentioned on page 246, indicating the weight of the newly born animal or child, it is obvious that the uterus itself must increase enormously in size. For instance, in the non-pregnant woman it is only about the size of the fist or less. At the end of pregnancy it is large enough to accommodate the whole of the baby and the fluid in which it floats, and it occupies the greater part of the abdominal cavity. Although the wall under these distended conditions is rather thin there is yet several times more tissue present than there was originally (fig. 99). The vagina also increases in size, otherwise the head of the child would be unable to pass.

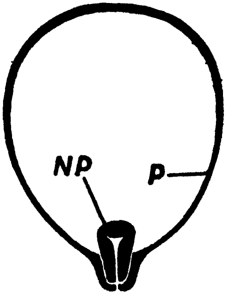

FIG. 99. The comparative size of the non-pregnant (NP) and pregnant (P) uterus. (After Corner, *The Hormones in Human Reproduction*, Princeton and Oxford, 1943.)

After the young have been delivered the most important accessory organs become the *mammary glands* (fig. 100). During pregnancy these have been enlarging so as to comprise more and more milk-producing tissue.

Shortly after the birth of the young this tissue becomes extremely active, and the minute pockets and conducting channels of the glands become distended with milk. They are continually emptied by the suction of the young on the openings in the nipple, which communicate by branching with all parts of the gland, and the milk which is removed is constantly replaced. It is manufactured from the tissue fluid and blood by the cells which form the walls of the secretory pockets or alveoli.

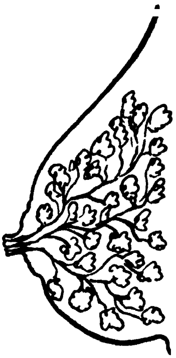

FIG. 100. The structure of the mammary glands. This is the same kind of structure as the pancreas and salivary glands, but instead of one duct there are several opening into the nipple.

We must now return to the ovary, about which we were talking when we digressed to describe the changes accompanying pregnancy in the accessory organs. The ovaries control the accessory sex organs by means of two hormones. These are *oestrogen* produced by the growing follicle, and probably by other parts of the ovary, and *progesterone* produced by the corpus luteum. The association of one hormone with the follicle and the other with the corpus luteum suggests that the action of progesterone is complementary, and that is in gėneral true. It is practically without action on any organ which has not been previously influenced by oestrogen. It is probable, however, that the ovary never stops secreting oestrogen, though it may produce less during the period when the corpus luteum is dominant.

In all animals a great many more eggs are produced than are fertilised and in most animals, including the human being, these eggs are actually discharged from the ovary at regular intervals. This means that in the absence of pregnancy there are regular cycles of ovarian activity in which the " follicular " phase, during which oestrogen is secreted, gives place to a " luteal " phase during which progesterone from the corpus luteum is dominant. When the ovum is not fertilised it very quickly dies and exerts no more influence on the cycle. The corpus luteum persists for a time (in women for about a fortnight) but does not last so long as the corpus luteum of pregnancy. Nevertheless it has time to exert some effect on the accessory organs and there are regularly recurring changes in them corresponding to the cycle of changes in the ovary.

During the action of oestrogen the lining of the uterus increases and thickens and the simple glands in it become correspondingly longer. After ovulation the effect of progesterone is seen, and the glands of the uterus become distended with secretion, while near the surface of the uterine lining large numbers of cells containing glycogen are packed. The lining of the uterus at this time becomes very freely supplied with blood. These changes are known as *progestational* changes because they are preparatory to gestation. The lining of the uterus is being prepared for the reception of a fertilised ovum. As we have said, the corpus luteum does not last very long when the ovum is not fertilised, and in the non-pregnant animal its degeneration is the signal for the disappearance of progestational changes. In some animals there is a fairly rapid shrinking of the lining of the uterus, while in others the breakdown occurs very suddenly with haemorrhage and the lining is disintegrated and dissolved and discharged via the cervix.

The action of oestrogen on the mammary glands is to cause them to increase in size and to expand their glandular tissue further, while that of progesterone seems to be to mature the glandular tissue and make it capable of secreting milk. It now seems possible that these effects may not be altogether due to the *direct* action of these substances, but to an indirect action through the anterior pituitary. Instead of doing all the work themselves they may stimulate the pituitary to do some of it. In pregnancy the amounts of oestrogen and progesterone which are circulating in the blood are enormous compared with those found in the normal ovarian cycle. In accordance with this we find that the mammary glands are not greatly affected during these cycles. They may increase and decrease in size a little.

It is highly probable in pregnancy that when the first stages have passed, and the foetus or foetuses are growing quickly with corresponding enlargement of the uterus, the amounts of oestrogen and progesterone capable of being secreted by the ovary and corpus luteum are insufficient. They are certainly produced in large quantities by the human *placenta*. The placenta represents that part of the growing embryo which does not become part of the future individual, but which has burrowed into the lining of the uterus so as to be freely washed by the maternal blood stream. After various changes of shape and structure it finally settles down to a disc-shaped mass of tissue embedded in the uterine wall and connected with the foetus by a cord containing blood vessels (fig. 101). Through these blood vessels the circulation of the foetus makes a kind of outside circuit, in the course of which it breaks up into capillaries in the placenta. These capillaries are themselves formed into small loops enclosed in little projections or villi which are

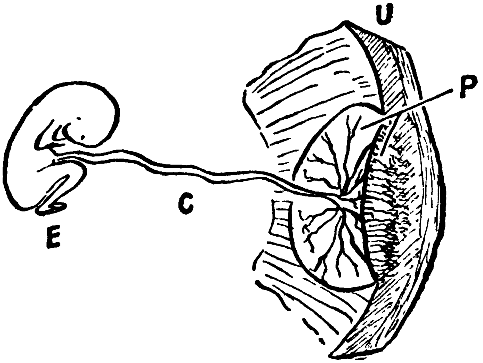

FIG. 101. Rough diagram showing how the embryo gets its nourishment and oxygen from the mother.

E, embryo. C, cord containing connecting blood vessels. P, placenta. U, wall of uterus.

in free contact with the maternal blood. The blood of the mother and the blood of the foetus do not mix, but exchanges of food and oxygen and waste products take place between them. When a baby is born this part of the circulation becomes useless to it. The cord is tied close to the baby so as to make sure that no blood will be lost, and cut. A short time later the foetal part of the placenta and that part of the uterine wall with which it is inextricably mixed (usually called the maternal part of the placenta) become detached and forced out of the uterus, which now goes into a strong contraction. This is important, because if it did not do so a large raw area where the placenta had been would be exposed and fatal bleeding might occur. The placental site also offers a ready port of entry straight into the blood-stream for micro-organisms, which goes a long way towards accounting for the rapidly fatal outcome too often associated in the past with puerperal fever.

Reproductive function in the male

Although the female germ cells mature and are discharged one by one, or in small batches, with a definite interval between each ovulation, the male germ cells are being continuously produced, except in those animals which fail to breed during certain times of the year. (In the female of these species ovarian cycles also cease.) The production of spermatozoa takes place in an organ called the *testis*, which is really a series of very thin tubes each about two feet long, coiled up and packed so as to take up relatively little space. They lead into another long coiled tube which finally turns into the duct—the *vas deferens*—by which the spermatozoa are led to the uretha (p. 214) The whole of this system of tubes acts as a store for spermatozoa, and a little sac (the *seminal vesicle*) on each side, which also has muscular walls, communicates with the duct and contributes a certain amount of fluid. So does a gland called the *prostate*. It is often stated that the mixture of this fluid together with that in which the spermatozoa are already suspended is beneficial to the sperm, but there is no very convincing evidence that this is so. The two main ducts finally open into the urethra through which, with some force, they expel their contents simultaneously with those of the seminal vesicle and prostate (fig. 102).

In addition to the sperm-producing mechanism in the testis, other cells of this organ produce a hormone—*androgen*—which

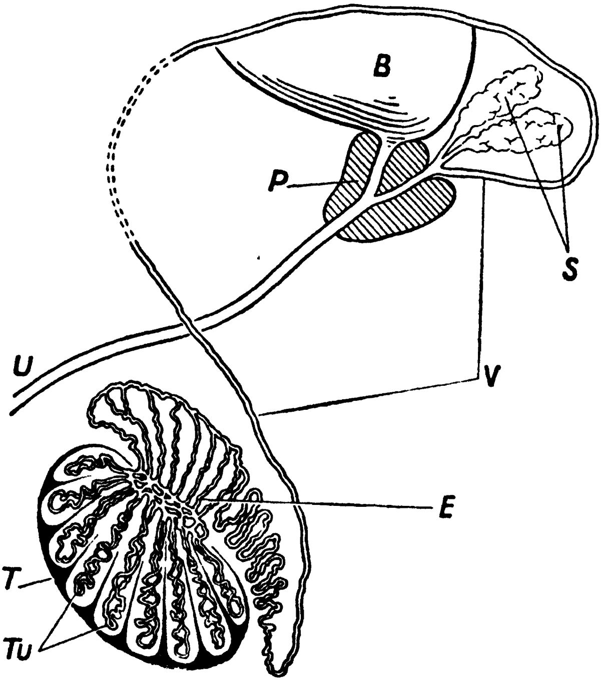

FIG. 102. Male reproductive organs.

T, testis. Tu, Tubules. E, epididymis. V, vas deferens. S, seminal vesicles. P, prostate. U, urethra. B, bladder.

they transfer directly to the blood-stream. This has the function of maintaining the accessory organs of the male, for example, the vas deferens, the seminal vesicle and the prostate. In the absence of the testes these organs degenerate. The distinction between the sperm-producing and hormone-producing tissue of the testis is very well shown by experiments in which the testes are placed inside the abdomen, where the temperature is higher than that to which they are normally exposed. The retention of testes in the abdomen sometimes occurs as an abnormality of development. In such experimental animals, or in such incompletely developed individuals, the tubules in which sperms are produced degenerate and the result is sterility. The hormone-producing cells, however, live quite happily and the accessory organs are kept in perfect condition. The secondary sex characters (see below) are also normal. This is quite different from the effect of removing the testes altogether, when the accessory organs and secondary sex characters remain undeveloped.

The secondary sex characters

Many parts of the body which have no direct connection with reproduction are influenced by the presence in the blood stream of the internal secretions of the ovary and testis. The effect of the hormones on such structures gives rise to what are known as secondary sex characters. Thus, in the human being we find that the distribution of hair on the body, e.g., the face, is different in men and women and the voice of men becomes much deeper. There are also differences in the skeleton, the bones of women being somewhat slighter than those of men and having in general a smoother contour, while there is a considerable difference in the shape of the hip bones. Further, the reason why muscles are not so prominent in women as in men is not so much because they are smaller, as that beneath the skin there is a layer of fat which has a considerable smoothing effect on the appearance of the outside of the body. Some of these differences are due to the presence of androgens in the male and some to oestrogens in the female. In animals the secondary sex characters are various and include the nature of the plumage of birds, the antlers of stags, the horns in some breeds of sheep and cattle, etc.

The anterior pituitary

The activity of the ovaries and testes, both in their germ-producing and hormone-producing capacities, is entirely dependent on the anterior pituitary. If this gland is removed, then the ovaries or testes shrink to small dimensions and cease to have any influence on the body. In such circumstances they can be restored by the injection of pituitary extract, and it seems fairly certain that there are two pituitary hormones involved. The first controls the ripening of the follicles in the ovary and the production of oestrogen and, in the testis, the production of spermatozoa. The second controls the formation of the corpus luteum in the ovary and the production of androgen in the testis.

In addition to this influence, which we might call the day to day function of the pituitary, it also has a long-term function. Thus, in immature animals, or in boys and girls, the ovaries and testes are clearly not fully functional. From about 13 to 15 years of age there is a quite rapid development in the activity of these organs, due to the fact that they are being stimulated by the pituitary. Why the pituitary should become more active at this time, which is known as the time of *puberty*, is not understood. We simply regard it as one of the facts of normal growth and development.

Some animals—in fact nearly all wild animals—have breeding seasons. That is to say, they are only sexually active during certain parts of the year. The connection with the seasons is obvious, though the precise nature of the influence of the environment has not been worked out in all cases. The duration of daylight and the change in temperature have, however, been shown to operate. It is believed that the environmental effects are appreciated first by the nervous system and result in the transmission of nerve impulses to the pituitary, thus stimulating it to activity. There are other instances of the effect of the nervous system on the pituitary. Thus certain animals, e.g. rabbits and cats, do not ovulate spontaneously. Crops of follicles in the ovaries grow and regress without the formation of corpora lutea, but if mating with the male occurs then the crop of follicles which is growing at the moment receives an additional stimulus from the pituitary via the bloodstream as a result of which it ripens fully, ovulates and gives place to corpora lutea. The stimulation of the genital organs through mating has initiated nerve impulses by which excitation has been transmitted to the brain, and from there to the anterior pituitary gland. These facts have been established by many ingenious experiments, including the removal of the pituitary gland of rabbits at certain intervals after mating.

Most animals will only mate at certain times during the breeding season and this depends on the cyclic activity of the anterior pituitary. It causes the ovary to secrete more oestrogen when the follicle is ripe, and this oestrogen, in addition to affecting the accessory organs in the way we have described, produces changes in the behaviour of the female animal, which is then said to be in heat. It is possible that oestrogen is not the only hormone involved but it is undoubtedly the chief one. Only when the female animal is in heat will she receive the male. In the human female, however, only the structural changes occur and there are no external indications of ovulation. The most obvious event in the human cycle is the haemorrhage at the end of the progestational phase.

The secretion of milk by the mammary glands is under the direct control of the anterior pituitary, which secretes a *lactogenic hormone,* sometimes called prolactin. Lactation can be induced in non-pregnant animals by injecting extracts containing this substance, while the mammary glands of lactating animals dry up immediately on removal of the anterior pituitary gland. It is thought that there is a further hormone controlling the growth of the mammary gland, the secretion of which is initiated by the presence of oestrogen or progesterone in the blood stream (see page 250).

CHAPTER XXI

THE SENSE ORGANS AND THE BRAIN

WE have discussed the mechanism of reflex action (pp. 71, 90) and gained a fair understanding of how events in various parts of the body could be co-ordinated so as to proceed to the advantage of the whole. Most of the reflexes we have mentioned have to do with maintaining the internal environment of the body constant in certain essential ways while giving different parts a considerable degree of individual freedom.

An animal lives, however, in an external environment with which, as an individual, it must also be in equilibrium. It is impossible to draw a sharp distinction between reactions to the external and those designed to maintain the internal environment, because the necessity for the latter is very often a consequence of the former. For instance, muscular activity is probably initiated in order to deal with something which is happening outside of the body, and the mechanisms thrown into play to ensure an increased oxygen supply to the active muscles without upsetting the internal economy of the whole body are an outcome of this.

An animal is in touch with its external environment chiefly through the sensations of touch (including the appreciation of hot and cold), sight, and hearing. In some animals, though not in man, smell is very important. Sensations are collected by *receptor organs*, of which those in the skin (fig. 103) require to be stimulated by direct contact, while the eye and the ear can receive stimuli which originate at a distance. The excitation of the various receptor organs causes impulses to pass up the afferent nerves which connect them to the central nervous system, and this excitation may be transmitted in the way we have described to muscles by means of impulses in efferent nerves. These straightforward paths of excitation give rise to rapid reactions, such as the instant dropping of an object which is too hot, the withdrawal of the foot from an injurious object, the rapid movement of the head and the closure of the eyes when a flying object rapidly approaches the face, and the similar evasive movement when something whizzes past the ear. It is true that we feel the heat in our fingers, and the pain in our foot, and we see or hear the objects which fly towards our head. But the immediate actions we take have nothing to do with the actual sensation. They are unconscious and depend on short paths through the nervous system, while the impulses leading to sensation travel by a longer path to the brain and are translated into consciousness. In other words, when the primary nerve impulses reach the central nervous system they set up excitation in more than one neurone, and these secondary impulses have different destinations.

In ordinary everyday life few sensations are sudden and unexpected. Our receptor organs, particularly the eyes and ears, are *continuously* passing information into the central nervous system, and the path to the brain becomes much more important than the reflex paths. The important element in the reaction of the body to these sensations is not speed, but a correct appreciation and ordering of the sensations themselves, their correlation with previous experience, and the initiation of appropriate activity by the brain. This more leisurely type of action is not only a desirable alternative to the simple reflex which, in preserving a limb, might place the whole body in jeopardy, but it actually reduces the number of occasions on which we are thrown back on our more primitive reactions.

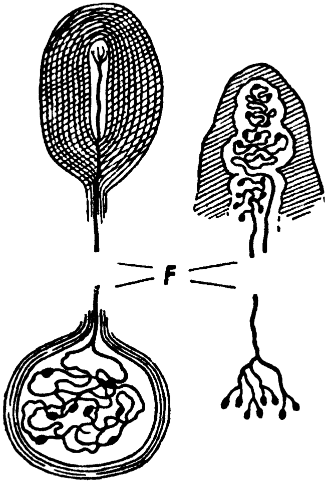

FIG. 103. Sketch of four sense organs found in skin and connective tissues. The difference in structure probably represents a difference in sensitivity to heat, cold, touch, pressure, etc. F, nerve fibre.

This is chiefly on account of the faculty which the eyes and ears have of appreciating *distant* stimuli, thereby enabling the body to avoid situations in which unpleasant or harmful stimuli impinge upon it without warning. It is clearly of advantage when crossing a road to be able to see and hear the traffic at a distance and choose the right moment for making the final move, rather than to set off without looking and rely on a series of prompt reflex actions to avoid the hazards which may be encountered.

This idea, however, deserves elaboration. Among the muscular movements initiated by the brain, those involved in speaking and writing are among the most important. We are so familiar with these activities that we sometimes tend to forget that they are essentially muscular movements, but very delicate and highly co-ordinated ones. By means of them we are able to convey our experience to other persons, and by interpreting the writing and speech of others we can make use of their experience. For instance, we do not stand in the bath and switch on an electric fire, because we know this may be fatal. Now we do not learn this by direct contact with the electric current nor does the sight of electrical apparatus in itself suggest danger to us. Neither our tactile nor our distance receptors are able to glean any direct warning from the objects themselves. We are nevertheless perfectly aware of the danger and we act upon it. This is because by using our eyes we have read, or by using our ears we have heard, of the danger. This would have been impossible if the information collected by eye-witnesses of fatal accidents, or from the victims of almost fatal accidents, hand not been translated at leisure by their brains into the complicated form of muscular activity which results in speaking and writing. By following out the train of thought suggested by this simple example it is easy to see that the whole of our civilisation and present mode of life is dependent on the high development and supreme dominance of non-reflex reactions to stimuli.

The high degree of organisation of the nervous system which is necessary for these reactions is reflected in the size of the cerebral hemispheres and the development of the neocerebellum. The microscopic structure of a part of the cerebral cortex is sketched in fig. 104 and it will be seen to consist of numerous layers of cells, each of which has connections with other cells. It will be recalled that the area covered by these cells and their fibres is greatly increased by the convolutions into which the surface of the brain is thrown. Some parts of the cortex are associated with certain kinds of sensation. When they are destroyed by injury or disease the corresponding sensation is found to be abolished or modified. The position of these areas is shown roughly in fig. 34. Injury to the motor area results in paralysis of voluntary movement, though certain involuntary movements may occur and local reflexes may be elicited from the limbs. The blank areas of the brain in fig. 34 are imperfectly understood, because if they are destroyed or damaged no easily defined defect such as blindness or paralysis occurs. There may be changes in memory and personality which, as they are very difficult to test in a patient, can rarely be assessed except on the basis of second-hand evidence.

One of the most important senses is very apt to be overlooked by the beginner. It is *muscle sense.* If as a result of very detailed information through the sense organs the body is going to make complicated movements, then each motor unit must know what every other motor unit is doing. This enormous mass of additional information is sent into the central nervous system from receptor organs in the muscle which record the degree of tension of its fibres. Some of it goes to the cerebral cortex, where it is interpreted and enters into consciousness, while some of it goes to the cerebellum which, as we have seen, is intimately connected with the motor cortex by a series of neurones passing upwards through the brain stem. The neurones responsible for initiating voluntary movement and passing down from the cortex to the local centres in the spinal cord are accompanied as far as the pons by numerous fibres

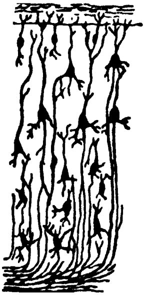

FIG. 104. Microscopic structure of cerebral cortex.

which terminate there against cells which pick up the excitation and transfer it direct to the cerebellum. The cerebellum thus receives information not only from the muscles, but also from that part of the cortex which is controlling them, and this presumably enables it to co-operate very precisely with the cortex in determining the pattern of excitation and inhibition. The indications are that this mechanism makes for smoothness and accuracy in voluntary movement, in which everything depends upon the pattern of excitation and inhibition in the motor centres of the spinal cord being exactly right, and waxing or waning at just the right speed. In disease or injury of the cerebellum voluntary movement is jerky and tremulous.

In the last paragraph we mentioned that muscle sense was appreciated and interpreted as a sensation in the brain, and this needs a little explanation because we are aware of no such " sensation ". We are, however, quite conscious of the exact position in space of any part of the body even when we have our eyes shut and cannot see where it is. We can generally grasp a familiar door-knob in the dark without fumbling and certainly if we can see an object we are able to close our eyes and touch it or grasp it without the least difficulty. This is because we know just where our hand is at any moment and it represents our *interpretation* of muscle sense.

Now that we have introduced this idea of interpretation we may go a step further. If we shut our eyes and someone puts an object into our hand, say an inkbottle or a matchbox or a penny, we can tell what it is without difficulty. This is because from the position and relative tension in the muscles governing the position of the hand and fingers we gain an idea of the shape of the object, from the touch receptors in the skin we learn whether the surface is rough or smooth, while from the temperature receptors we learn whether it feels cold, like a coin, or neutral, like a matchbox. Also, from the degree of tension in the muscles of the hand and arm and from the actual force with which the object presses the skin against the underlying bone we gain an impression of the weight of the object. We do not think of all these attributes one by one. We simply grasp the object and say " This is a matchbox "—or a penny or an inkbottle. By simultaneously taking cognisance of all the various bits of information about the object which it is receiving, the brain is able to combine them in such a way that we receive what appears to be a single impression of its nature.

If we now incorporate the distance receptors into this integration of sensation and we think more particularly of the eye, we find that we gain an even better insight into the world around us. We can recognise a matchbox in the way we have described in the last paragraph with our eyes shut. But if we use our eyes we can recognise a matchbox without touching it at all. At some time in our early life we have looked at matchboxes and handled them and have correlated the two sets of impressions so that either vision or handling will now serve our purpose. This extends to nearly all objects in our immediate environment, so that by looking at a thing a very definite impression of what it would feel like is conveyed to our mind. Similarly, if we handle an object blindfolded we have a very good impression of what it would look like. These deductions would be impossible had we not previously done a great deal of investigation in which we used vision and manipulation simultaneously.

The high degree of co-ordination between hand and eye is by no means confined to stationary objects. In fact, most of our skilled pursuits depend on the enormous advantage this co-ordination gives us in dealing with moving objects. Thus, in playing tennis or cricket we gauge the position in space of the rapidly moving ball by means of vision, and this is combined so accurately with our muscle sense and the other components of the system controlling our voluntary muscles, that we are able to move the racket or bat to a precise spot where we know the ball will be at the moment when we wish to strike it. By means of our visual apparatus, therefore, we see the world not as a flat picture, but in three dimensions.

It is customary in books of this kind to describe the eye and the ear in some detail because they are very remarkable organs, and their structure is of interest in itself. It is more important, however, to know what contribution they make to our normal existence and to ask ourselves how they are able to do so. While giving a brief description of the eye, therefore, we must bear these two questions in mind. How does the eye tell us the relations of objects to each other and how does it record the relation of objects to our selves, particularly if they are moving?

The Eye

The eye is a roughly spherical structure (fig. 105) enclosed in a tough fibrous capsule, the sclerotic, with a circular transparent window in the front. With the exception of the front part of the sphere, the sclerotic is lined by a layer of darkly pigmented tissue which need not concern us,containing blood vessels and nerves, and inside that by a layer of nervous tissue, the *retina* which contains the actual end organs of vision. They are called

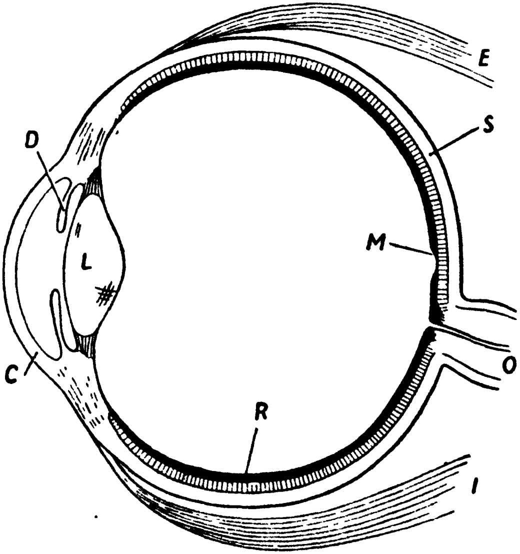

FIG. 105. Diagrammatic section through the right eye seen from above.

C, cornea. S, sclera. R, retina. M, macula lutea. L, lens. O, optic nerve. D, iris. I and E, muscles respectively pulling eyeball inwards and outwards.

" rods " and " cones " on account of their shape when viewed through the microscope (fig. 106). There are over 100 million rods and more than 6 million cones, and between them they furnish a sensitive surface on which the light falls. Each bit of the image on the retina is, by means of these numerous receptors, reported to the brain, and the conception of a complete object is due to the brain's interpretation of the impulses passing into it.

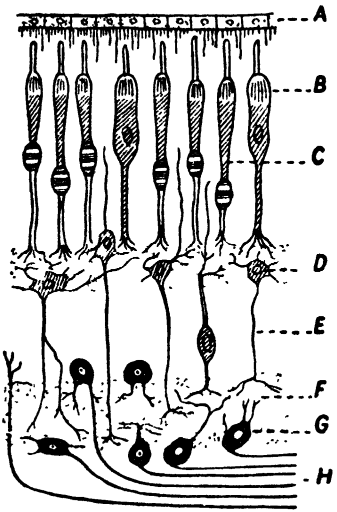

FIG. 106. Microscopic appearance of the retina.

A, pigment cells. B, cones. C, rods. D, F, feltwork of nerve fibres. G, ganglion cells. E, axon of cells in layer D. H, nerve fibres of optic nerve. Note that the retina is very thin and the direction of light is from below upwards in the diagram.

We do not know how this interpretation is brought about any more than we understand the previous examples of interpretation which we have given. But we do find that in the area of the brain to which the visual impulses go (fig. 34) each part of the retina is represented, so that if part of the visual cortex is injured, then a definite part of the retina is rendered useless. It is very interesting to find that different parts of the retina are not equally represented in the cortex. That part—the *macula lutea*—on which the light from an object is focused when we look straight at it accounts for a great part of the visual cortex although it is but a spot on the retina. Examining this spot in detail, however, we find that it is almost entirely composed of cones which are packed tightly together and each of which has a separate fibre to carry its impulses to the brain. In other parts of the eye the excitation from several receptor organs converges on to a single fibre.

The cones are responsible for acuity of vision in daylight, and when we want to see anything distinctly we turn our eyes so that the light from it falls on the macula lutea. The cones also perceive colour. As we travel over the retina in any direction from the macula, the cones become less and less numerous and we find a greater and greater proportion of rods. The rods are thought to be chiefly responsible for our ability to see in very dim light, a function which they cannot perform without a supply of vitamin A. If we look directly at a dim star at night it disappears, but if we then look at an adjacent star the original one reappears. Every time we try to look carefully at it, it disappears again. This is because our attempt at careful examination causes the image of the star to fall on the macula lutea and the light is too dim to stimulate the cones which are the only receptors there. Directly we move the macula so as to focus some other star in the vicinity, the light from the first star is focused on a part of the retina containing rods, and, although we cannot see it so distinctly as we should like, we do know quite definitely that it is there.

The Optical System of the Eye

The way in which images of objects are focused on the retina is of interest and some practical importance.

If we wish to indicate in a diagram that a ray of light passes from one point to another, we can join the two points by a straight line. If, however, we magnify our diagram, the line becomes thick and our ray becomes a beam. If we regard the beam as having thickness we find it easier to visualise what happens when it passes from one transparent medium into another. Light travels more slowly in some transparent media than in others; for instance, its velocity in water is only three-quarters of its velocity in air.

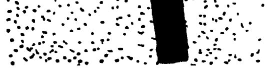

FIG. 107. Deflection of a beam of light entering a denser transparent medium from another at an oblique angle.

When a beam of light passes from air into water or glass, it continues in a straight line if it strikes the dividing surface perpendicularly. If it strikes it obliquely, however, it is deflected, and a good way of remembering the direction of the deflection and working out its consequences is to imagine that, in the beam depicted in fig. 107, the lower edge begins to travel more slowly while the corresponding points on the upper edge are still going at the same speed, which they maintain until the whole beam has entered the denser medium. We may imagine that the temporary retardation of the lower edge compared with the upper edge causes the beam to swing downwards, and the greater the inclination of the surface against which it strikes, the further it swings.

The reader will find that the more he thinks in detail of this description of the deflection of light, the less satisfying it becomes, and unless he has made a special study of optics he is advised just to use the general idea as an aid to memory.

Now rays of light entering the eye pass from the air into a second transparent medium of which the window in the front of the eye—the *cornea*—is made. The surface of this window is shaped like part of a sphere so that every ray of light from a point outside, with the exception of the one absolutely perpendicular to it, strikes it obliquely (fig. 108). The further away the rays are from the central one, the more inclined are they to the surface of the cornea. Therefore, if we imagine a "pencil" of rays coming from a point, those round the edge of the pencil will be deflected the most when they strike the cornea, and there will be all degrees of deflection until the central ray is reached, which is not deflected at all.

Behind the cornea is some fluid—the *aqueous humour*, and in the posterior part of the eye is a semi-fluid transparent medium—the *vitreous*. There is not much difference between the optical densities of the cornea, the aqueous and the vitreous, so if we only had these to deal with we could imagine the deflected rays entering the cornea and continuing without further deflection until they met in a point inside the eye. At this point there would be an image of the outside point from which the rays started. In actual fact it would need a cornea, etc., of greater optical density or a much longer eye than we

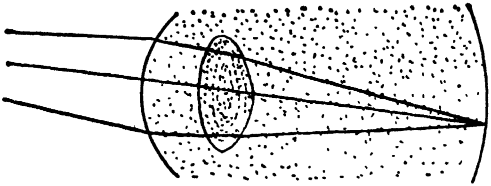

FIG. 108. The path of rays of light through the eye. It is assumed that the substance of the cornea, the aqueous and the vitreous cell have the same optical density and that the lens has a greater optical density. The rays are therefore deflected at the outer surface of the cornea, and at each surface of the lens, but as the change in optical density is greatest at the first surface, this is where the maximum deflection occurs. The true state of affairs is more complicated, since the optical densities are all slightly different, and furthermore, the centre of the lens is denser than the outside, so the path of a ray within it is curved. A much simpler optical system which would give the same result, is employed as the basis for practical calculations.

possess for these rays to come to a focus inside it. An additional converging mechanism is interposed between the aqueous and the vitreous in the form of the *crystalline lens*. It has a greater optical density than the media in which it is suspended, and its surfaces are also spherical in contour. Rays of light striking its anterior surface, therefore, are further deflected and while they are passing through the transparent substance of the lens are approaching each other more rapidly than before. When they strike the back surface of the lens and pass back into the less dense medium they are deflected still further in the same direction. That is to say, the outer edge of the beam enters the less dense medium before the inner edge and, therefore, proceeds faster, until the corresponding point on its inner edge has also emerged. The total effect of all these surfaces at which the rays become deflected or *refracted* is to bring them to a focus on the retina (figs. 107, 108).

Since the light from each point of an object is focused in the same way, a complete but greatly reduced image is formed on the retina. It must be obvious from our diagrams that objects further away will be brought to a focus at a point nearer to the front of the eye than nearer objects. But the rods and cones which lie perpendicular to the surface of the retina have a certain length. They can simultaneously accept focal points which are not quite in the same plane, i.e. a far object may be focused on the front end of a cone while a nearer object is equally well focused at the back end of another cone. The way in which this works out in practice reduces itself to a problem in geometry, but the fact is that when we look at a landscape everything beyond a distance of about eight yards is focussed at the same time. As objects become nearer, however, they become increasingly out of focus unless the eye accommodates itself. *It does this by an alteration in the shape of the crystalline lens, the anterior surface of which bulges somewhat.* The increased refraction which can be produced by this means enables objects to be seen quite clearly until they are within about ten inches of the eye, but at this short distance there is very little depth of focus, that is to say, when we are looking at a picture in a book eighteen inches away, anything slightly nearer or slightly farther away from the eye will be out of focus.

The mechanism of accommodation and stereoscopic vision

Fluid (the aqueous) is forced into the eye from certain parts rich in capillary blood vessels and it drains away through channels we need not describe. The relative pressures of entry and exit, however, are such that a certain *intra-ocular pressure* is maintained, which keeps the eyeball tense. Now the crystalline lens is attached to the outer wall of the eye by fibres which radiate from its circumference, so that the intra-ocular tension keeps it stretched, i.e. in its flattest shape, suitable for seeing distant objects. Where the suspensory fibres enter the wall of the eye there is an elevation on its surface and beneath this are smooth muscle fibres. In order to accommodate the eye for near vision, these muscle fibres contract in such a way as to make this elevation higher, i.e. the points all round the eye at which the suspensory fibres are attached move nearer to the lens. The lens itself is always tending to take up a more spherical shape, i.e. when the *ciliary muscle* is at rest, the lens is forcibly pulled by the intra-ocular tension from the shape it woud assume if it were removed from the eye.

The ciliary muscle is thrown into action by impulses passing down the third cranial nerve. They are the result of excitation brought by certain connections of the optic nerve to the centre in the midbrain from which the third nerve arises. The nature of these connections is rather complicated and the cerebral cortex is probably involved in the reflex path. That is because the stimulus initiating the reflex is not simple like the heaviness of touch, the loudness of sound or the intensity of light, but is a whole constellation of light stimuli which when integrated result in a composite stimulus which gives the information " in focus " or " out of focus ". It is unlikely that this type of integration, so intimately related to conscious sensation, could occur anywhere but in the brain, and from here it is presumed that corresponding impulses pass down to the appropriate nucleus of the third nerve.

The third nerve also contains fibres which arise from a slightly different area of the midbrain and which supply (together with two other cranial nerves) the muscles which move the whole eyeball in the orbit. The centre controlling these fibres is also thrown into action by the accommodation reflex in such a way that the eyes swing inwards. This brings the particular object which is being looked at into focus on the macula of each eye. If both eyes remained looking straight ahead, the rays of light from a near object would fall on the outside part of each retina. A third motor component of this reflex is a constriction of the pupil, which controls the amount of light entering the eye. The pupil itself, which is the small black disc in the centre of the eye, is merely an aperture through which all the light reaching the retina passes. The coloured ring surrounding it is the *iris*, an opaque diaphram, which contains smooth muscle and which can contract or relax on instructions from the nervous system, according to the amount of light falling on the retina. For various reasons concerned with the scattering of light in optical media, the size of the pupil controls to some extent the sharpness of the image which is formed.

The convergence of the eyes which takes place during accommodation raises the question of whether it is of any advantage to have two eyes instead of one. By the simple expedient of covering up one eye for an hour or two it will readily be appreciated that one eye is not so useful as two eyes. The chief reason is that we cannot easily judge the distance of objects from us. We have to rely entirely on whether one thing is obviously in front of another, i.e. obscuring part of it, or whether its shadow falls on other objects, or, if we are familiar with it, what its size is in relation to its surroundings. We could probably tell whether a man was close to us or far away because we know that objects in the distance look smaller, and if a man appears small we conclude that he is a long way off.

When we use two eyes we have important and critical information on this question of distance. There are six muscles controlling the movements of each eyeball and it must be obvious that the arrangement of impulses passing in from their tension-recording receptors is quite different when both eyes are directed to a near object from what it is when they are both directed towards a far object. For every slight change in the angle between the optical axes of the eyes the impulses passing up from the twelve muscles concerned will be differently arranged. We also get a slightly different view of an object from each eye, as can readily be demonstrated by looking at something and closing first one eye and then the other. The fusion of the two images into one composite image takes place in the brain in some way which is not understood, but it must be clear that the two views are much more different in the case of a near object

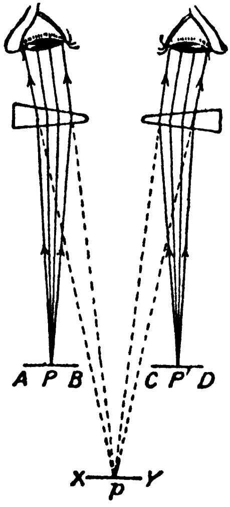

FIG. 109. Diagram of a stereoscope.

Two photographs, APB and CP'D, are seen combined at XpY. The rays of light from APB and CP'D are refracted by the prisms into the eyes so that they appear to come from XpY.

than in the case of a far object. A detailed consideration of this problem is far beyond the scope of this book, but it is possible to understand that this sensory adjustment as well as the muscular one contributes to our estimation of distance.

It is well known that the fusion of images enables us to see objects in three dimensions or as we say " stereoscopically ". In the instrument known as the stereoscope, the light reflected from two slightly dissimilar photographs of the same object or landscape is directed into the eye, by specially shaped lenses, in the same direction in each eye as it would have taken had it been coming from the real objects. The picture then springs to life and we get a three dimensional impression of it (fig. 109).

The Ear

Since we have gone at some length into one special sense organ, the eye, we shall not devote much space to the ear. The reader is referred to text books of physiology for a detailed description. In man the visible part of the ear has little or no function, but animals can move their ears so as to turn them towards the direction of the sound. The tube, whose opening

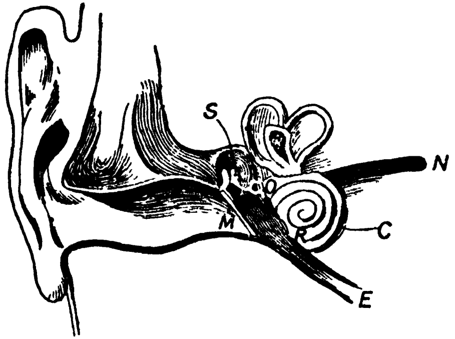

FIG. 110.

M, Tympanic membrane. S, Chain of ossicles. O, Oval window of C, Cochlea. R, Round window. N, Auditory nerve. E, Eustachian tube is visible and which is about an inch and a quarter in length, ends in the ear drum, a membrane which closes it completely at its inner end. On the other side of this is a cavity known as the middle ear, communicating with the throat by the *eustachian tube* which opens periodically so as to make the pressure in the middle ear equal to atmospheric pressure. Embedded in the dense mass of bone which lies on the inside of the middle ear is the real receptor organ for hearing, the *cochlea* (fig. 110). It is essentially a spiral tube full of fluid, but divided into three compartments by a bony shelf and two membranes arranged as in figs. 111 and 112. Sitting on the horizontal membrane are receptor cells, with microscopic hairs projecting from the top of them making contact with a projection on the bony shelf which overhangs them.

When sound waves fall upon the eardrum they cause it to vibrate and the vibration is transmitted by a series of levers (very minute bones) to the compartment labelled *A* in fig. 111. This compartment begins in a hole in the inner wall of the middle ear which is closed by a curtain, and the curtain is attached to the inner end of the lever system. The vibration of the fluid in this compartment causes the whole of the fluid in the cochlea to vibrate, and it is thought that this general movement is made possible by the fact that the lower compartment (*B*, fig. 111) also ends in a window in the middle ear which is closed by another curtain. This is not attached to anything but the edges of the window and by bulging allows the to and fro movement of fluid to take place. The oscillation makes the two membranes *A* and *F* (fig. 112) vibrate and the hairs of the sensory cells are distorted by their movement against the over-hanging shelf of bone. This initiates nerve impulses in the nerve fibres which

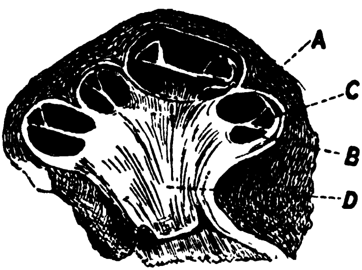

FIG. 111. The bony cochlea sawn in half.

A, The scala vestibuli. B, The scala tympani. C, The membranous canal of the cochlea. D, the central pillar of the cochlea. (After Kölliker.)

lead from the sensory cells into the central nervous system, and these impulses are interpreted as sound.

The cochlea is so minute that it is quite difficult to find out exactly how it works, i.e. how we are able to appreciate different pitches and qualities of sound. However, the *basilar membrane* consists largely of fibres running from the bony shelf to the wall of the cochlea, and these are of different lengths (curiously enough they increase in length as the apex of the spiral is approached). They are also thought to be stretched to different degrees. Now the vibration of fluid which we have described is probably very slight, and it is possible that it does not throw all the fibres of the basilar membrane into vibration, but only those which are " in resonance " with the sound waves falling on the ear at any particular moment. According to the pattern of the vibration in the basilar membrane we interpret sound as high-pitched or low-pitched and of various qualities.

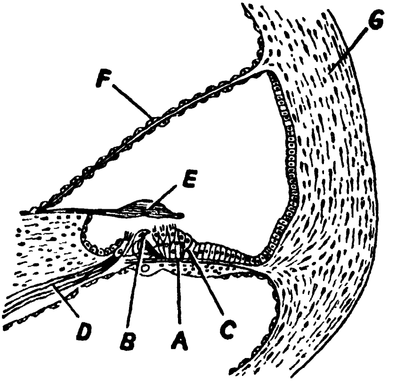

FIG. 112. Section through part of the cochlea showing the membraneous canal of the cochlea.

A, Basilar membrane. B, Rods of Corti. C, Hair-cells. D, Nerve-fibres. E, Membrana tectoria hanging over the hair-cells. F, Membrane separating off the membranous canal of the cochlea. G, The wall of the cochlea. (After Retzius.)

The saccule, utricle and semi-circular canals

These organs are also hollowed out of the bone on the inner side of the middle ear, and are in close relation to the cochlea. The whole collection of organs is known as the labyrinth, and when they are revealed by taking away the solid bone surrounding them (fig. 113) they have the appearance of a single organ. However, those parts of the labyrinth other than the cochlea are not, so far as we know, at all concerned with hearing. The bony cavities are lined by a membrane which contains fluid, and the motion of this fluid stimulates receptor organs. Here similarity with the cochlea ceases. The receptor organs are not arranged in any sort of continuous keyboard as in the cochlea, but are located at various strategic points in the cavity (fig. 113). The sensory cells of the organs carry very long " hairs " which may be stuck together by a kind of jelly or they may contain particles of chalky material. When the head is turned rapidly the fluid tends to lag behind and although it may not actually move, the pressure becomes temporarily greater at some points than others, and the constellation of impulses passing from the sensory cells to the brain is altered. Some of the end organs are distorted by their own weight when the head is moved out of the horizontal position, so that even if it is held steady in a natural posture, the fact is recorded and appreciated by the brain.

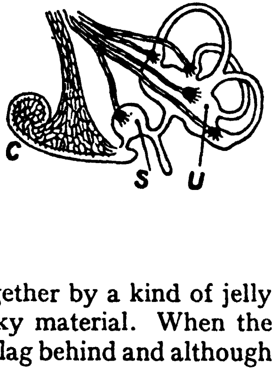

FIG. 113. Diagram of the membraneous internal ear, removed from the bony internal ear and showing the branches of the auditory nerve.

C, Membranous canal of cochlea. S, Saccule. U, Utricle. There is shown one nerve ending in the ampulla of each semicircular canal, one in the saccule, and one in the utricle. The nerve-endings extend throughout the length of the cochlea.

These organs are very much more important in animals than in man, for we rely greatly on our eyes to tell us where we are in space. Nevertheless, the organs of equilibrium have wide connections in the brainstem and the information which they transmit is correlated with that coming from the tension receptors and the muscles in such a way that the pattern of reflex contraction in the muscles maintains our equilibrium.

Conditioned Reflexes

We have tried to show how information from the various sense organs is integrated by the brain to form an impression, and we have tentatively assumed that each sense organ was helping to analyse the appropriate part of a composite picture, the picture being the external environment. The facility with which the brain connects impressions from different sense organs was shown many years ago in a very striking fashion by the Russian physiologist, Pavlov. It is impossible in this short space to do justice either to his work or to more recent work on the same lines, but it is too interesting and important to pass over altogether even in an introductory account.

The basis of the experiments is always a well-established reflex, such as the secretion of saliva by the salivary glands on placing food in the mouth. A dog will invariably produce saliva in response to such a natural stimulus, but we should not expect him to do so in response to a flash of light, the stroke of a gong or a touch on the skin or any other inappropriate stimulus. Nevertheless, it is quite possible to build up such an abnormal reaction. If a dog, carefully isolated from unwanted stimuli, hears the sound of a gong every time he is given food, then the stimuli passing from the ear to the brain become connected with the centres controlling the secretion of saliva. After the repetition of the double stimulus a sufficient number of times, it is found that the dog will secrete saliva when the gong is struck even if no food is presented. A response, very often called a " conditioned " reflex, has been, as it were, manufactured. The linking-up of sensory impulses with motor or secretory effects has been shown to be possible with a wide variety of sense and effector organs which would ordinarily be quite unrelated to each other.

The phenomenon is chiefly of interest to us as a clear demonstration of a very high type of integration in the nervous system. It is a long jump from such carefully controlled experiments as these to everyday life, but such findings are seen to be of great interest to physiologists and psychologists when it is remembered how many associated sense impressions we are exposed to for the whole of our lives. The experimental demonstration of even the simplest laws of association clears the ground somewhat for the investigation of the obscure relationship between brain and mind.

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